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MALARIA.

UNITED FRUIT COMPANY, BOSTON, MASS. TWENTIETH ANNUAL REPORT. MEDICAL DEPARTMENT. 1931. Section I. pp. 17–33, and Section II. pp. 34–111.—[**Papers on Malaria.**]

i. **Comments on some of the More Important Diseases occurring in the Tropical Divisions.** [CONNOR (R. C.)] pp. 3–33. [Malaria, pp. 17–33.]

Dr. R. C. Connor, the General Manager of the Company's medical department, reports that malaria is the most prevalent disease in the estates. By strenuous efforts its incidence can be reduced to proportions which do not materially handicap the community, but eradication seems impossible. The results of antimalarial measures have been "somewhat gratifying," but fall very short of what was hoped for. Control measures are greatly handicapped by the obstructive attitude of the natives, who refuse to take drugs unless they are actually suffering from symptoms of malaria. The principal antimalaria measures adopted are :—(*a*) Careful selection of sites, and clearing for a radius of 200 yards around dwellings; (*b*) Removal, or Paris green treatment, of breeding places; (*c*) Periodical surveys and treatment of infected persons with one plasmoquine tablet and 10 grains of quinine twice a day for six days ; when the infection rate in a camp exceeds 25 per cent., the whole population is subjected to treatment. The screening of quarters and the use of mosquito nets are generally speaking impracticable on the Company's plantations.

Several of the medical officers were supplied with atebrin for experimental purposes. A total of 320 cases was treated. The usual course was a single dose of 0·3 gram daily for five days ; larger doses over longer periods were given in some instances without producing any symptoms beyond a yellow staining of the skin, and that in only a few cases. Photosensibility did not occur. Drs. CORDES and DE LA TORRE of Preston, Cuba, in reporting the results of treating 121 cases, stated that they had never seen more than two paroxysms occur after the initiation of atebrin treatment ; all the patients made an uneventful recovery. Drs. NEUMANN and LE DOUX, of the Company's hospital at Santa Marta, Colombia, reported concerning atebrin that "the treatment of 75 cases of aestivo-autumnal and tertian malaria has given us the rather spectacular result of curing all the patients within one week or less." They detected atebrin in the urine as long as 36 days after the last dose, and concluded that its slow elimination rendered it suitable for prophylaxis. Very few relapses were observed after atebrin treatment, but local conditions made it impossible to follow up many of the patients.

Drs. PHELPS and JANTZEN, of the hospital of Puerto Castilla, Honduras, treated 14 cases of blackwater with atebrin, and in no instance did it provoke another attack.

ii. **Observations on the Diagnosis and Treatment of Malaria.** [JAMES (Wm. M.)] pp. 34–41.

Dr. W. M. James contributed a paper on the value of the thick film method, and claimed that by it 30 per cent. more films are found positive than when thin films are employed. The films should be dried at room temperature and stained in Giemsa solution for 15 or 60 minutes according to the strength of the stain (see GREEN, this *Bulletin*, Vol. 29, p. 718).* Dr. James could always find parasites by this method when the patient's temperature was over 100°, if the fever was due to malaria. It is one of the most reliable tests in medicine because, " if in competent hands it is negative on two occasions twelve hours apart, then the condition is certainly not acute malaria." In the author's experience, subtertian cases are invariably fatal when more than 15 per cent. of the cells contain parasites : between 5 and 10 per cent. the outlook is serious. He believes that in malaria it is important to attack early with plenty of quinine.

iii. **Anopheles Mosquito Control.** [HALE (Carleton).] pp. 98–107.

Mr. Carleton Hale, the Company's General Sanitary Inspector, stated that with mechanical dusters there is an enormous saving of Paris green and labourers' wages, as compared with hand-dusting. A 3 per cent. mixture (by volume) is used in the dusters, and lime, limestone or soapstone are employed as diluents.

[References to 10 other papers on malaria contained in this Report are given in the list of Titles of Unnoticed Papers on pp. 92–6.]

W. Fletcher.

PEREPEREZ, LARA (Gutierrez), BOTE, ZOZAYA, CARTAÑÁ, TORRADEMÉ & COLLADO (Gil) sous la direction de G. PITTALUGA. Le paludisme dans les "deltas." (Etudes sur certaines conditions naturelles et expérimentales de l'anophélisme dans le delta de l'Ebre, 1926–1930.) [**Malaria in Deltas. Treatment of Malaria.**] —*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1932. Mar. Vol. 5. No. 1. pp. 5–131. With 5 plates, 1 chart, 16 graphs & 29 figs. [21 refs.]

ZOTTA (G.). Etudes sur le paludisme dans le delta du Danube. (I : Anophélisme sans paludisme.)—*Ibid.* pp. 133–176. With 1 map.

CIUCA (M.), BALTEANU (J.), BAILLIF (L.), IRIMESCO (G.), ALEXA (E.), CONSTANTINESCO (N.), JANCOU (J.), AGAPI (C.) & VIERU (M.). Contribution à l'étude du traitement du paludisme.—*Ibid.* pp. 177–208. With 10 charts. [11 refs.]

SLATINEANU (Al.), BALTEANU (I.) & ALEXA (I.). Recherches comparatives sur l'action thérapeutique de la quinoplasmine, du quiniostovarsol et de la quinine sulfurique dans le paludisme spontané.—*Ibid.* pp. 209–237.

The Malaria Commission of the League of Nations has recommended for special study the problem of malaria in the deltas of great rivers.

*In the summary of GREEN's paper on p. 719, line 8, *for* "to three drops of (b)" *read* "to three cc. of (b)."

In this volume, Professor Pittaluga describes the conditions in the delta of the Ebro, and Dr. G. Zotta describes those in the delta of the Danube. The only Anopheles found at the mouth of the Ebro are the two races of *A. maculipennis*: the long-winged *A. maculipennis maculipennis*, and the short-winged *A. maculipennis atroparvus*; of these, the first-named is much the more abundant. Moreover, anopheles are more plentiful in stables and pig-styes than in human habitations. Among a large number examined 83 per cent. contained animals' blood, 9 per cent. avian blood, and only 6 per cent. human blood. The distribution, numbers, and food preferences of anopheles were studied by means of six experimental huts built at chosen spots and baited with various animals or birds. One interesting point which emerged was the great attraction of warm-blooded animals for anophelines; even in places where birds were abundant and animals very scarce, 80 per cent. of the anophelines contained animal blood: very few female anopheles were caught in huts baited with poultry. It was found that there was dissociation between the resting places of anopheles and their sources of food at certain times of the year. Female anopheles take shelter far from their food-supply during the period of dispersion in the summer, but when hibernation approaches they shelter near their food. Years ago, the delta was poor, little cultivated and almost uninhabited. There was much malaria then, but during the last 25 years the fertile land has been exploited, and there are now 14,000 hectares of rice-fields and market gardens; although the rice-fields breed myriads of anopheles, the position is entirely changed, and in 1930 the spleen rate was only 8.

Dr. Zotta describes conditions in the delta of the Danube, which affords another example of anophelism without malaria. The anopheles feed on beasts and birds rather than on man, and at times this propensity becomes a veritable misanthropy. There are sporadic cases of malaria, but though there is an abundance of anopheles which are potential carriers the disease never spreads.

Dr. Ciuca and his colleagues contribute a study on the comparative values of quinine bihydrochloride, cinchonine hydrochloride and sulphate, an Amsterdam sample of quinetum (containing 20 per cent. of amorphous alkaloids and 35 per cent. of cinchonidine), and two samples of cinchona febrifuge differing widely in composition. They found that the quinetum was as efficacious as quinine, but that the cinchonine salts and the febrifuge were inferior.

Dr. Slatineanu and his colleagues report on the therapeutic action of quinine, quiniostovarsol, and quinoplasmine. There was little difference between these drugs as regards action on schizonts; but quinoplasmine destroyed gametocytes. Relapses were 37 per cent. with quinine, 24 per cent. with quiniostovarsol, and 10 per cent. with quinoplasmine.

W. F.

RECORDS OF THE MALARIA SURVEY OF INDIA. Calcutta. 1932. June. Vol. 3. No. 1. pp. 1–173. With numerous illustrations.

i. **Malaria in Calcutta.** [COVELL (G.)]. pp. 1–82. With 1 graph, 3 maps, 1 chart & 5 figs. [58 refs.]

Major G. Covell contributes an interesting paper on malaria in Calcutta. It is not, to-day, the serious menace to health which it was many years ago. *A. stephensi* is the transmitting agent in the central parts of the city. The water supply from the Hoogly is intermittent,

and this necessitates the use of an enormous number of cisterns and receptacles in which *A. stephensi* breeds. The water-carriage system has greatly increased the number of breeding places in recent years. Breeding places of *A. ludlowii* have been found at various points within 12 to 30 miles of Calcutta, and there is evidence that this species has been recently introduced into these localities by country boats. There is danger that *A. ludlowii* may gain a footing in the Salt Lakes to the east of the city. These were formerly tidal and thus unsuitable for breeding, but they have become non-tidal in recent years owing to river silting, and any scheme designed to restore tidal influence should be regarded as an important anti-malarial measure. (See IYENGAR, this *Bulletin*, Vol. 29, p. 334.)

ii. **Malaria in Patiala State.** [COVELL (G.).] pp. 83–101. With 2 maps.

Major Covell also gives an account of a survey of some towns and villages in Patiala State. *A. culicifacies* is considered to be the carrier in the plains, and *A. listoni* in the foot-hills where malaria is most severe.

iii. **Malaria in Sind. Part VIII. Malaria in Shahbandar Division, Karachi District, Sind.** [COVELL (G.) & BAILY (J. D.).] pp. 103–124. With 1 map.

Major Covell and Subadar J. D. Baily record the results of a survey, made during two weeks in September 1931, in the Shahbandar division of Sind, which forms part of the delta of the Indus. The northern part is fertile rice country, but the southern part is barren and consists of sand hills, mangrove swamps and salt waste. As a whole it is highly malarious, The chief carrier is *A. culicifacies* which breeds in irrigation canals, borrow-pits, and collections of water drained off from rice fields. The large lakes are comparatively harmless.

iv. **River-Sand Silting and Other Antimalarial Measures in South Sylhet, Assam.** [STRICKLAND (C.) & MURPHY (R. A.).] pp. 125–142. With 5 plates, 4 figs. & 2 maps.

Professor C. Strickland and Dr. R. A. Murphy describe the successful control of malaria on several estates in South Sylhet, Assam, by the reduction of mosquito breeding. In some places this was accomplished by diverting silt-laden hill-streams into swamps, thus filling them up and converting them into productive agricultural land. In other places, swamps were drained by ditches protected by a covering of vegetation, and contour drains were made along the slopes.

v. **Some Findings in a Malaria Survey carried out on a Group of Tea Estates in the Sibsagar District of Assam from August 1, 1930, to July 31, 1931.** [MANSON (D.) & RAMSAY (G. C.).] pp. 143–160. With 1 map and 2 graphs.

A survey of a group of tea estates in the Sibsagar district of Assam, from August 1930 to July 1931 was made by Dr. D. Manson and Dr. G. C. Ramsay, under the auspices of the Ross Institute. *A. minimus* was the only mosquito found to be infected. Silt prevents its breeding. In places where the water remains clear during the malaria transmission season much man-made malaria has resulted from blocking the natural drainage with bridges, culverts and the like. Clearing dense shade from streams has also favoured the breeding of *A. minimus*.

This species breeds in fairly clear water, slowly running or stagnant, exposed to sunlight or under partial shade. Perennial rivers and streams are endemic breeding grounds except when they become silt-laden during the monsoon. Other breeding places are rice fields lying fallow, drinking-water reservoirs, and drains carrying clear water. [See also RAMSAY and SAVAGE, p. 88.]

vi. **Confirmation of *A. philippinensis* as a Malaria Carrier in Bengal.** [BOSE (K.).] pp. 161–162.

Mr. K. Bose, Honorary Secretary of the Birnagar Palli Mandali contributes a paper confirming the finding by Dr. P. SUR that *A. philippinensis* is a carrier in Bengal.

vii. **Some Experiments to determine the Efficacy of Wire Gauze Screens of Different Apertures in excluding Anopheline Mosquitoes in India.** [MULLIGAN (H. W.) & MAJID (Abdul).] pp. 163–169. With 1 fig.

Captain H. W. Mulligan and Jemadar Abdul Majid conclude that an aperture of 0·055 inch square in gauze screens is sufficient to exclude *A. culicifacies*, *A. listoni* and *C. fatigans*.

viii. **Ultraviolet Absorption Spectra Studies in Malarial Sera.** [KEHAR (N. D.).] pp. 171–173. With 4 figs. on 2 plates.

Mr. N. D. Kehar has studied the ultraviolet absorption spectra of normal and malarial sera. He found that whereas no new bands were developed in malarial sera, there was a general dimming of the spectra, and the results suggest that though no new constituents can be detected in the ultraviolet region, there is evidence of quantitative changes. *W. F.*

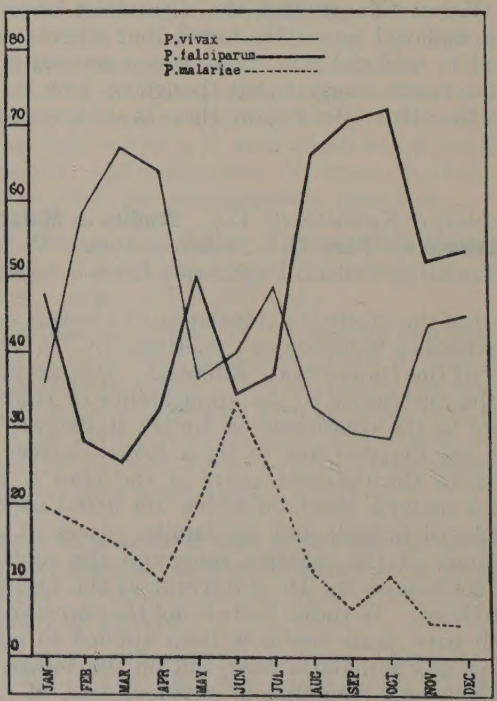
WHITE (R. Senior) & NEWMAN (C. D.). **Studies in Malaria as it affects Indian Railways. Part II.**—*Technical Paper No. 258.—Part 2.* 71 pp. Calcutta: Central Publication Branch. [As. 14 or 1s. 6d.]

The first part of this study is a translation of a lecture delivered at the "Advanced School of Malariology" in Rome by Dr. FILIPPINI, Chief Health Officer of the Italian State Railways; the second part sets out the views of the authors as to the applicability of Italian methods of malaria control to the conditions on Indian Railways. In Italy, the malaria zones are mapped out under a Royal decree, and thus the malarial status of the different parts of the lines is known. Each employee has a malaria sheet on which are noted particulars of the malarial attacks of himself and his family, places of residence, etc. The delimitations of the malaria zone and the malaria census of employees is considered by Dr. FILIPPINI as the first requisite for a rational prophylaxis. In India, there is not the necessary staff for this. Screening with wire gauze has now been applied to all buildings on Italian railways in the malaria zone, but on the Indian railways it is virtually non-existent. Quinine is supplied free of charge to the employees of Italian railways, and is issued for prophylaxis on a large scale. The authors are not in favour of prophylactic quinine in India, but they consider the treatment of the sick is one of the most important means of prevention. "Adequate quininization is a *sine qua non*, . . . something more palatable than quinine in solution must be provided . . . this means quinine in tablet or cachet form . . . for children,

one of the tasteless salts in a chocolate coating." As regards anti-larval measures, the authors consider them more suited to the tropics of Asia than to other parts of the world. The carrier anophelines of India have a very restricted range of flight in comparison with those of Europe, and " the gradual realization of this fact, and its final admission in their report, was one of the most interesting things to watch during the recent tour of the Malaria Commission of the League of Nations." Although the range of Indian anophelines is comparatively small, antilarval measures limited to railway land alone would be insufficient, and, in the absence of screening and effective treatment, would not give such good results as in Italy. *W. F.*

IYENGAR (M. O. T.). **Seasonal Incidence of Tertian, Subtertian and Quartan Infections.**—*Indian Jl. Med. Res.* 1932. July. Vol. 20. No. 1 pp. 303–326. With 8 charts.

The author examined 1,876 positive films, during sixteen months commencing June 1930. The patients were people attending a treatment centre at Singur in the Hoogly District. The three species of parasites occurred in the following proportions :—*P. vivax* 41·8 per cent., *P. falciparum* 50·3 per cent., *P. malariae* 14·4 per cent. The seasonal incidence was as follows :—*P. vivax* highest in March and April, and



Comparison of the seasonal incidence of the three forms of malaria in an intensely endemic area in Bengal. Subtertian infections are high from August to October, and tertian infections from February to April. Quartan infections are highest from May to July, but their incidence is small compared with the other two types of infection.

[Reproduced from the *Indian Journal of Medical Research.*]

ranging from 29 to 67 per cent. of the total infections ; 49 per cent. of the patients carried gametocytes. *P. falciparum* highest in September and October, ranging from 25 to 72 per cent. of total ; 41 per cent. carried gametocytes. *P. malariae* highest in June, ranging from 4 to 33 per cent. of total ; 64 per cent. carried gametocytes. *W. F.*

JAFAR (M.). **Malaria in Mingaladon Cantonment, Burma.**—*Indian Med. Gaz.* 1932. Sept. Vol. 67. No. 9. pp. 493–498. With 1 map & 2 graphs.

Mingaladon is situated 12 miles north of Rangoon. It was cleared of jungle, and troops moved into it in 1928. It was regarded as malaria-free, like Rangoon ; but in 1930 there were a few cases, and in 1931 there were 37 fresh infections and 109 relapses. Suspicion fell on *A. hyrcanus*, and the author found two specimens infected out of 95 examined. *W. F.*

ANDERSON (Drysdale). **Notes on Mosquito-borne Diseases in Southern Nigeria : III. Differences in the Periodicity of Various Mosquitoes.** —*Jl. Trop. Med. & Hyg.* 1932. Oct. 15. Vol. 35. No. 20. pp. 305–308. With 7 graphs.

The author's conclusions are as follows :—The periodicities of the breeding intensities of *A. costalis*, *A. funestus*, *A. hargravesi* and *A. nili*, all of which mosquitoes occur in Abeokuta, differ among themselves. The curves of *A. costalis* and *A. nili* can be explained on what is known of their breeding habits. These are not enough to explain the curves of *A. funestus* or of *A. hargravesi* which are influenced by some conditions at present not known. *W. F.*

GIBBINS (E. G.). **Natural Malaria Infection of House-frequenting *Anopheles* Mosquitoes in Uganda.**—*Ann. Trop. Med. & Parasit.* 1932. Oct. 29. Vol. 26. No. 3. pp. 239–266. With 6 figs.

Only two of the six species of Anopheles incriminated as vectors of malaria in Uganda were encountered in more than one region ; these two were *A. costalis* and *A. funestus*. *A. costalis* is the most dangerous, and at Kampala, 18·6 per cent. showed infection ; 6,836 stomachs and 6,486 salivary glands were examined. At Jinja, the infection rate was 17·8, and at Mbale 24·2. The distribution of this mosquito is governed principally by temperature ; it is common about the warm sunny towns at 4,000 feet, and when temperature is favourable its prevalence depends on rainfall. *A. funestus* is the most abundant malaria carrier in Uganda. The infection rate at Kampala was 14·8 per cent. ; 5,853 stomachs and 5,665 glands were examined. *A. marshalli* was found in the high country surrounding Fort Portal (5,000 feet), where *A. costalis* is seldom found in the wet season, and 0·3 per cent. were infected. *A. theileri* and *A. moucheti* were found to be important vectors of limited distribution : *A. theileri* in one district near Kampala, and *A. moucheti* on the river near Jinja. *A. pharoensis* occurred only on the lake shore near Jinja, where 5·9 per cent. were infected. *A. mauritianus* and *A. transvaalensis* frequent native dwellings in which goats are kept ; none were found infected. *W. F.*

BARTOLUCCI (Filiberto). La malaria in Somalia. [**Malaria in Somaliland.**]—*Arch. Ital. Sci. Med. Colon.* 1932. Oct. 1. Vol. 13. No. 10. pp. 630–632. English summary (3 lines).

This short paper consists of general statements on the prevalence and character of malaria in Somalia; actual figures are not given, beyond the somewhat vague statement, "according to recent statistics malaria affects about 15 per cent. of the population" It is widespread generally throughout the interior, the coastal regions with the exception of Juba being practically free. The regions of highest incidence are along the rivers Uebi Scebeli and Juba, where it is particularly prevalent at the times of flood and rains. The commonest species of anopheles are *A. quadrimaculatus* and *A. costalis* which together constitute 38 per cent. of anophelines; others less frequently encountered are *A. funestus* and *A. barbirostris*. *P. falciparum* and *P. vivax* predominate, the quartan parasite is rare. Clinically, the chronic form is most common, with splenomegaly but often without fever.

H. H. S.

SERGENT (Etienne). Epidémies de paludisme en Algérie. [**Epidemics of Malaria in Algeria.**]—*Arch. Inst. Pasteur d'Algérie.* 1932. Mar. Vol. 10. No. 1. pp. 22–33. With 13 figs.

The author concludes, from observation of the epidemiology of malaria in Algeria over a period of 29 years, that the principal cause of the epidemics is excessive rainfall—not so much the total quantity, as the extent of surface water which remains at the beginning of the summer. The annual variations of malaria are not entirely dependent upon meteorological conditions, but are influenced by other factors at present unknown. The great epidemics recur at intervals of about 12 years.

W. F.

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1931** [WILSON (Christopher J.), Chairman]. —21 pp. 1932. Kuala Lumpur: Govt. Press.

The question of periodic suspension of anti-malaria oiling on estates was discussed, and it was stated that though in certain selected cases, the practice was justified, it was nevertheless highly injudicious to suggest in general terms to the public, or to inexperienced medical officers, that any relaxation in anti-malarial measures was permissible.

The results of a model drainage scheme carried out under government supervision on a rubber estate were considered. The annual cost of maintenance was £4 13s. an acre, and the anti-malaria Engineer stated that skilled supervision was absolutely necessary for the success of subsoil drainage systems. The Chief Health Officer pointed out that as much as 10 per cent. of an estate had to be kept clear of trees, in order that their roots should not destroy the sub-soil drains; he had considerable doubts whether sub-soil drainage was suited to agricultural areas.

W. F.

ANIGSTEIN (Ludwik). **Malaria and Anophelines in Siam. Report on a Study Tour.**—*Quart. Bull. Health Organisation, League of Nations.* Geneva. 1932. June. Vol. 1. No. 2. pp. 233–308. With 18 figs. & 1 map on 10 plates. [17 refs.]

Siam may be divided into three parts as regards the incidence of malaria—(1) Central Siam consists of a huge plain extending from the

head of the Gulf of Siam to a length of 350 kilometres and a breadth of 150. It is one of the richest rice-fields in the world. There is very little malaria either in this alluvial plain, or in the delta where Bangkok is situated. There is little mosquito breeding in the large straight irrigation canals, because the water is changed periodically by the tide and carries too much silt ; but there is much breeding in those parts of the irrigation system which are cut off from the source of the supply, and where the water is stagnant. There are vast numbers of culex, stegomyia and mansonioides, and also of such anophelines as *A. barbirostris, A. hyrcanus* and *A. vagus* ; but, apart from a few *A. fuliginosus* and *A. aconitus*, malaria carriers are absent. (2) This zone consists of ranges of hills which bound the fertile plain, except on the north-east where it is separated from French Indo-China by the Mekong River. The inhabitants of the hill country live by cultivating rice among the foothills, but it is difficult for them to grow enough to support themselves. Malaria is prevalent and severe. The finding of *A. listoni, A. culicifacies* and *A. minimus* in association with hyperendemic malaria makes it probable that they are the carriers. They are found in clear slowly-flowing streams and in the irrigation channels of the terraced paddy-fields when these form short branches of clear streams. *A. maculatus* is found occasionally. It is recommended that the alluvial valleys between the hill-ranges should be irrigated in order to permit rice-cultivation there, instead of in the foot-hills. The irrigation streams would become silty, thus preventing the breeding of dangerous anopheles, and the economic condition of the people would be improved. Malaria parasites were found in the blood of 108 children in the following proportions : *P. malariae* 40·8 per cent., *P. falciparum* 34·5 per cent., *P. vivax* 27·7 per cent. (3) In the south, there is a long narrow strip of country connecting the widest part of Siam with the Malayan peninsula. The eastern shore of this strip faces the Gulf of Siam, the western shore faces the Indian Ocean ; down the centre, runs a range of mountains. Malaria in the central hilly region is severe, and occurs in association with stream-breeding *A. listoni* and *A. minimus*. There is a moderate amount of malaria along the shore, probably due to *A. ludlowii*. There is also some malaria in the cultivated areas further inland, associated with *A. aconitus* and sometimes with *A. culicifacies*. *W. F.*

FENG (Lan-Chou). **Investigations on Malaria and its Transmission in Amoy, Fukien Province, South China.**—*Jl. Trop. Med. & Hyg.* 1932. July 1 & 15. Vol. 35. Nos. 13 & 14. pp. 198–202 ; 214–221. With 3 figs., 1 plate, 1 map & 1 chart. [31 refs.]

Malaria frequently causes much sickness among the rural population. There are two rainy months, April and August ; the malaria curve goes up with the rains, reaches its maximum a month later, and then declines. The disease is very prevalent near the hills, less so in the villages more distant from them, and rare in the town of Amoy. This survey was made in July-August, and at that season *A. minimus* was the commonest anopheline. It was found responsible for an epidemic of malaria among a group of imported labourers working near the foothills ; 29·85 per cent. of the mosquitoes showed oöcyst infection, and 8·57 per cent. showed gland infection. In the villages, oöcyst infection was present in only 4 per cent. *A. hyrcanus* var. *sinensis* may also be a carrier at other seasons. *A. maculatus* is considered an important

carrier in Hong Kong on epidemiological grounds, but no infected specimens have been found in any part of China ; the author caught no adults in Amoy but bred one specimen from a larva.

The author's method of examining salivary glands is to transfer them to a drop of salt solution on a slide ; remove almost all the saline with a pointed piece of filter paper ; make a smear about half a centimetre wide with a little piece of cover-glass ; examine almost dry without a cover-glass ; the sporozoites appear as slightly-curved, refractile rods. Such smears stain well with Romanowsky stains.

W. F.

SOERONO (M.), LALLEMANT (G. F. M. Avé) & SOESILO (R.). De stand van de malaria in de Tjiheavlakte. [**The State of Malaria in the Tjiheavlakte District, Java.**]—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1932. Vol. 21. No. 2. pp. 21–27. English summary.

In the years 1891–1904, the Government irrigated 13,600 acres for rice cultivation, at a cost of five million guilders. The results were satisfactory at first, but owing to insufficient drainage the soil became water-logged ; as a result of this the crops were poor, and malaria was prevalent owing to the breeding of *A. aconitus* in the irrigation water. MANGKOEWINTO recommended that the rice-fields should be allowed to run dry after the harvest, and that only one crop should be grown in a year. The execution of this plan has been followed by great improvement. *W. F.*

DE BUCK (A.), SCHOUTE (E.) & SWELLENGREBEL (N. H.). **Further Investigations on the Racial Differentiation of *Anopheles maculipennis* in the Netherlands and its Bearing on Malaria.**—*Riv. di Malariologia.* 1932. Mar.–Apr. Vol. 11. No. 2. pp. 137–156. With 2 charts & 7 figs. on 1 plate.

The original differentiation into long-winged paucidentate, and short-winged multidentate races is useful as a means of rapid orientation in an unexplored area, but it allows of nothing beyond a statistical differentiation ; the size, especially, is dependent on the food of the larvae. In order to breed mosquitoes as large as they are found in nature, single larvae must be reared in separate small jars, and fed on dried, powdered Daphnia, unicellular algae and piscidine. There are other morphological differences which are of great value, because they are unmodified by the usual methods of laboratory breeding. (1) In full-grown larvae, the average number of branches which the ante-palmate hairs possessed between them on the same side of the 4th and 5th segments was : in shortwings 5·9, and in longwings 9·3. (2) Ventral claspette spines with rounded tips were found in 0·3 per cent. of male shortwings, but in 40 per cent. of longwings. (3) The film spreading between the ribs supporting the egg-floats (intercostal film) is smooth in shortwings, but shows a network of minute crossbars in longwings.

Biological characters are even more important in distinguishing the two races : (*a*) the longwings will not copulate in captivity, but the shortwings do. (*b*) During hibernation, it is difficult to induce longwings to feed, and if they are persuaded to do so, the blood forms a contracted clot at the lower end of the stomach, with a clear transparent upper

end, and the insect will not feed again. The shortwings feed readily, the blood does not clot firmly at one end of the stomach but fills the whole of it and is quickly digested so that the mosquito is soon ready for a second feed. [Excellent photographs are given, illustrating these conditions.] (*c*) The clotting of the blood in the longwings makes them more difficult to infect because the oökinetes cannot reach the stomach wall. In one experiment, the salivary infection of longwings was 27 per cent. as compared with 68 in shortwings. In another experiment, the average number of zygotes in the stomach of longwings was only 11, as compared with 70 in shortwings. In the spring and summer, it is as easy to infect one race as the other. (*d*) The shortwing is a brackish water-breeder, and the longwing is confined to fresh water, yet, strangely, the shortwing when in captivity prefers to oviposit in fresh water, while the longwing is indifferent whether it is fresh or salt. If long and shortwinged larvae are bred out together in salt water, the advantage is with the shortwings, and they predominate in the resulting adults. [See this *Bulletin*, Vol. 29, p. 345.] *W. F.*

Gabriel (Josef). Le paludisme et l'anophélisme en Russie Subcarpathique. [**Paludism and Anophelism in Subcarpathian Russia.**]—*Travaux Inst. d'Hyg. Pub. Etat Tchécoslov.* 1932. Apr. Vol. 3. No. 2. pp. 23–31. With 1 map & 4 figs. on 1 plate. [10 refs.]

In some districts of the part of Czechoslovakia (Subcarpathian Russia) examined, anophelism occurs without malaria, and the presence of the two races of *A. maculipennis*, according to de Buck, Schoute and Swellengrebel (see above), was established. (1) The large, long-winged, light-coloured, malaria-indifferent race predominated. Only 3 per cent. were engorged with blood, but 86 per cent. contained hypertrophied fat bodies. (2) The small, short-winged, dark, many-toothed, malaria-active race showed 62 per cent. engorged and only 28 per cent. with enlarged fat bodies. The two races are not separate species, but merge into each other through intermediate forms. Excellent photographs of the wings and maxillary teeth are given. *W. F.*

Djaparidse (P. S.). Zur Frage der Gattungsimmunität bei Malaria. [**Species Immunity in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Sept. Vol. 36. No. 9. pp. 476–478.

Working in a malarious district in Georgia the author studied the question amongst parasite carriers of all three species of malarial parasite. His results are recorded in two tables. These show the percentage of carriers of *P. vivax*, *P. malariae* and *P. falciparum* at various age periods from birth to 60 years. From one district 150 carriers and from another 482 were selected in compiling the tables. Migration of population in these endemic areas was absolutely excluded. The tables show that the percentage of carriers of *P. vivax* falls gradually with increasing age, whilst the percentage of carriers of *P. falciparum* increases. In the case of *P. malariae* such a correlation is not observed. He proceeds to explain the results. He considers that in the case of *P. vivax* a mild or " labile " infection of the organism takes place and this infection may remain in the body for years without producing signs of disease except enlargement of spleen. The presence of the parasite protects against a super infection with the same species ; hence as age advances, this species will be less frequently met with on

examination of the peripheral blood. On the other hand the *P. falciparum* causes immediately severe clinical signs and leaves the organism comparatively soon ; this brings about an almost complete disappearance of protective power against this species, so that with increasing age in endemic areas the parasite carriers are found to increase. *E. D. W. Greig.*

Malaria-Commissie uit den Gezondheidsraad. Jaarverslag over de Jaren 1930 en 1931 van de Malaria-Commissie uit den Gezondheidsraad [Aldershoff (H.), Chairman]. [**Annual Report for 1930 and 1931 of the Malaria Commission of the Ministry of Health.**]—Reprinted from *Verslagen en Mededeelingen betreffende de Volksgezondheid.* 1932. July. 27 pp. With 2 charts (1 folding).

The Commission have decided against the practical value of anti-larval measures for a country like Holland with its irrigation system and abundance of water. Thorough treatment of the sufferers from malaria, prevention of entry of mosquitoes to houses and destruction of those which have already entered are the measures recommended. An exceptional opportunity for putting these into practice is afforded by the Zuyder Zee reclamation project. Reference is made to what are called control stables in the malaria campaign. These stables, placed in malaria districts, have been used over a long series of years for the collection of mosquitoes and the variation in monthly numbers caught provides a valuable seasonal index of prevalence. Perhaps the most interesting part of the report is the account of experiments in malaria therapy carried out in the country district of Franeker and in Wormeveer. In Franeker from 1928 onwards the treatment of malaria consisted of 1 gm. quinine sulphate daily for 14 days and then 1 gm. daily every 4 days for 3 months. The same protracted treatment was used for each case of relapse. With this treatment relapses were numerous. From July 1929 the treatment was changed to 1 gm. quinine daily for 7 days and the same for each relapse. A more rapid occurrence and some increase of relapses was the result but the cure-rate remained very much the same. By July 1930 a commencement was made of treatment with a combination of plasmoquine and quinine which Sinton had found in British India to reduce the relapse rate from 50 per cent. to 10 per cent. Chinoplasmine tablets (300 mgm. quinine sulphate and 10 mgm. plasmoquine) were administered for two weeks in a dose of 3 tablets per day. The result was astonishing. Not one of the 44 primary malaria cases showed a relapse and only one recurrence took place among the 22 relapse cases. Little or no unpleasant symptoms attended the administration. As a control on this operation we have the results in the town of Franeker itself, where quinine therapy alone was practised and where relapses occurred as usual. The bright prospect opened up by this experiment was somewhat dimmed by the experience at Wormeveer. In this case 3 tablets of chinoplasmine were administered to adults and less to children for a full week, beginning in March 1931. Altogether 82 primary cases of malaria were treated and 39 of these suffered from a relapse in the same year. " Further observation is certainly necessary."

The report concludes with an adverse criticism of some of the conclusions reached by James from a study of the results obtained with

artificially induced malaria, especially the contention that tertian malaria should exhibit a daily rise of temperature but by an immunization process only shows fever every second day. *W. F. Harvey.*

MARTINI (E.). Grundsätzliches zur therapeutischen Malaria. [**Fundamentals of Therapeutic Malaria.**]—*Dermat. Woch.* 1932. Oct. 22. Vol. 95. No. 43. pp. 1548–1552.

The editors asked the author to give his opinion on malaria therapy from the point of view of the malariologist. He is inclined to consider that the attitude in Germany towards malaria therapy is too casual. Accordingly he takes the opportunity of underlining the risks, both to the patient and the community, which may attend this form of treatment. To obviate these risks he enumerates a series of precautions, which in his view, are essential. Amongst the risks to the patient he mentions that experience has shown that malaria aggravates many other diseases, in particular tuberculosis. [This is not in agreement with the work of KYRIASIDIS, this *Bulletin*, Vol. 28, p. 118.]

E. D. W. Greig.

D'HERELLE (F.). **Clover and Malaria.**—*Amer. Jl. Hyg.* 1932. Sept. Vol. 16. No. 2. pp. 609–617.

This paper is written as a reply to the criticisms of the author's hypothesis made by Bruce MAYNE and by STRATMAN-THOMAS. (This *Bulletin*, Vol. 25, p. 557; and Vol. 29, p. 344.) This hypothesis is that the "primary cause of anophelism without malaria is the coexistence in a region of plants pertaining to the genus *Melilotus*, or to another genus presenting the same property, related as it seems to the presence of coumarin in the honey" on which the mosquitoes feed. When the author first published this hypothesis in 1924, he suggested that the glucoside might play a rôle in insects comparable to that which quinine plays in man. He now considers that its action is not plasmodicidal, but that the parasites are gradually attenuated until the disease disappears. In favour of the hypothesis are cited :—(*a*) The freedom of those parts of the Argentine Republic where a scented clover "*trebol de olor*" a variety of *Melilotus*, grows. (*b*) The disappearance of malaria from certain islands of Zealand, and from the northern provinces of Holland which coincided with the accidental introduction of Melilotus (*c*) The freedom from malaria of those parts of Egypt where clover is grown. *W. F.*

KNOWLES (R.) & GUPTA (B. M. Das.). **Clinical Studies in Malaria by Cultural and Enumerative Methods. Second Series.**—*Indian Med. Gaz.* 1932. Aug. Vol. 67. No. 8. pp. 432–446. With 5 charts. [12 refs.]

The histories of 20 cases of malaria are given with daily parasite counts and temperature readings; in most cases a Bass culture was made at the end of the period of observation, in order to confirm the results of microscopic examination. In several of the benign tertian and subtertian cases, spontaneous cure occurred; "this is often, or perhaps usually, followed by relapse." In quartan cases, the infection tended to persist, and spontaneous cure did not occur; a feature of the early stages was high fever associated with so few parasites that they might

easily have been missed in thin films. The authors suggest that the number of gametocytes produced is dependent on some factor in the host's metabolism. They consider that one of the most important problems in malaria is a study of the biological factors—individual, climatic and other—associated with variations in gametocyte production. They used atebrin in the treatment of several cases, with excellent results ; but a four-day course of atebrin cost three times as much as a ten-day course of quinine. A patient in whom the laevo-rotatory quinine and cinchonidine produced haemoglobinuria was successfully treated with the dextro-rotatory alkaloid quinidine.

W. F.

Earle (Walter C.) & Perez (Manuel). **Enumeration of Parasites in the Blood of Malarial Patients.**—*Jl. Lab. & Clin. Med.* 1932. Aug. Vol. 17. No. 11. pp. 1124–1130. With 1 fig.

This is a modification of Thomson's method (*Ann. Trop. Med. and Parasit.* 1911–12, Vol. 5, p. 471) which the author prefers to that of Sinton. Ordinary pipettes graduated in cubic millimetres are cut into sections long enough to handle 10 cmm., and are drawn out into fine points, not too small to admit a fine wire. An area 3 by 15 mm. is drawn on a piece of paper which is placed under a glass slide. Ten cubic millimetres of blood are drawn up into the pipette and 5 cmm. are spread over this area on the slide. The resulting thick film is stained with Giemsa. Beginning at one end of the smear, all parasites are counted, in a band, to the other side. Every fifteenth such band is counted so that the sum of the parasites gives the number present in 1/15 of 5 cmm. The pipettes are cleaned with water. The end of the pipette is not wiped after taking up the blood, because as much blood sticks after the spreading of the slide as before. *W. F.*

James (S. P.), Nicol (W. D.) & Shute (P. G.). *Plasmodium ovale* **Stephens : Passage of the Parasite through Mosquitoes and Successful Transmission by their Bites.**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 139–145. With 2 charts.

In 1922, Stephens described *Plasmodium ovale*, studied in blood from East Africa, as a new species. In 1927, he confirmed and extended his description in a case from Nigeria. In 1930, Warrington Yorke and Uvedale Owen showed that the morphological features of the asexual stages of the parasite remain constant when it is passed from person to person by direct blood inoculation. The authors, working with a strain from the Belgian Congo, succeeded in infecting *A. maculipennis* and in transmitting the infection to patients by means of these mosquitoes. They found that the morphological characters of the parasite in its asexual stage were unaltered by passage of the infection through mosquitoes, and that the arrangement of the pigment in young oöcysts was absolutely distinctive. They conclude " that there remains no doubt that *P. ovale* is a separate species, and that its morphological characters in the human and insect hosts are characteristic and constant." [See this *Bulletin* Vol. 20, p. 296, and Vol. 28, p. 606.] *W. F.*

Benhamou (Ed.). Paludisme et splénectomie. [**Malaria and Splenectomy.**]—*Bull. Soc. Path. Exot.* 1932. July 6. Vol. 25. No. 7. pp. 685–690. With 3 figs.

Details are given of four cases of splenectomy for splenic anaemia in persons who had formerly suffered from malaria. The operation was followed by recrudescences of the malaria which were very resistant to treatment with quinine and other drugs. The author concludes that splenectomy removes a defensive organ. Adrenalin caused parasites to appear in the blood of splenectomized patients; consequently its action in this respect is not solely dependent upon the production of splenic contractions. *W. F.*

Jemma (R.). Klinische Feststellungen ueber die Malaria der Kinder. [**Symptomatology of Malaria in Children.**]—*Arch. f. Kinderheilk.* 1931–32. Vol. 95. Nos. 3/4. pp. 227–241.

The author considers that there are profound differences in the clinical picture of malaria in adults and children. The younger the child the more impossible it becomes to detect the classical and well-marked clinical picture of malaria. For a correct diagnosis the medical man has to appreciate a series of symptoms. He discusses these in detail as they manifest themselves in the various systems, digestive, nervous, etc. He then considers the atypical forms of malaria and finally the complications. He considers of special interest the relation between malaria and tuberculosis. Malaria definitely aggravates the course of tuberculosis and in malarial children the medical man must keep a vigilant outlook for early signs of tuberculosis. [This view is not in accordance with the observations of Kyriasidis (this *Bulletin*, Vol. 28, p. 118).] *E. D. W. Greig.*

Giglioli (George). **Clinical Notes, Autopsy and Histopathological Findings from Five Fatal Cases of Quartan Malarial Nephritis from British Guiana.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1932. Aug. 11. Vol. 26. No. 2. pp. 177–187. With 4 figs. on 1 plate.

Daniels first drew attention to the prevalence of nephritis in the Colony; his figures were based on the results of postmortem examinations. The report by Grace, No. 3 of the Memoir Series of the London School of Hygiene and Tropical Medicine [this *Bulletin*, Vol. 29, p. 73] tends to give a misleading impression by minimizing the importance of this disease in British Guiana. Giglioli [this *Bulletin*, Vol. 28, p. 131] has already drawn attention to the almost specific role of the quartan parasite in the etiology of nephritis, which follows chronic, untreated malarial infection. In the earlier cases, the kidneys are enlarged, the cortex is thickened, and the lesions are prevalently degenerative. In old cases, typical, secondarily contracted kidneys are found, and the lesions are prevalently inflammatory and proliferative. Quartan malarial nephritis presents much the same characters as the nephritis caused by pyogenic infection. *W. F.*

Surbek (K. E.). Beitrag zur Kenntnis der Malaria-Nephritiden. [**Malarial Nephritis.**]—*Schweiz. Med. Woch.* 1932. July 16. No. 29. pp. 664–666. With 1 fig. [29 refs.]

In a table the author sets forth his observations on 15 cases of nephritis caused by quartan malaria occurring in Sumatra. The course

of the disease is subacute or chronic and the symptoms definite. Oedema and ascites are constantly present. Albuminuria is marked. Anaemia is pronounced and there is often an intense infection with *Plasmodium malariae*. If the renal damage is not too advanced the cases respond very well to quinine and the renal symptoms clear up rapidly, He refers to the work of GIGLIOLI in British Guiana (this *Bulletin*, Vol. 28, p. 131) on malarial nephritis. He also discusses acute malarial nephritis due to malignant tertian and mixed infections of malignant and benign tertian. Oedema is not a marked feature of these cases. The blood urea is raised. He has never found in these cases parasitized red cells in the urine. He has never observed a case of acute malarial nephritis pass on to haemoglobinuria. When quinine is administered early the renal symptoms clear up quickly. He notes that nephritis is very rare in inoculated malaria and that might suggest that the nephritis and malaria are not causally connected, but he considers that the favourable conditions under which the inoculated patients are treated accounts for the absence of renal complications.

E. D. W. Greig.

TAYLOR (K. P. A.). **A Valuable Sign in the Differential Diagnosis of Acute Abdominal Malaria.**—*Amer. Jl. Med. Sci.* 1932. Nov. Vol. 184. No. 5. pp. 699–707. [15 refs.]

Alarming abdominal symptoms sometimes occur in malaria ; such cases are usually of the malignant tertian type. They may be differentiated from cases of acute abdominal lesions by the two following signs :—(1) In malaria, macroscopic or occult blood is nearly always present in the gastric contents, and (2) there is absence of involuntary abdominal rigidity. *W. F.*

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE. 1932. Aug. 11. Vol. 26. No. 2. pp. 105–138. With 13 charts.—**Synthetic Antimalarial Remedies and Quinine. Discussion** [JAMES (S. P.), HENRY (T. A.), SWELLENGREBEL (N. H.), DALE (Henry), PRAIN (David), NICOL (W. D.), MANSON-BAHR (P.), SCHULEMANN (Werner), WATSON (Malcolm), CASTELLANI (Aldo)].

Col. S. P. JAMES.—The aim of large-scale antimalarial effort by means of drugs is to provide an abundant, cheap remedy available to the whole population of malarious countries preferably by growing cinchona in these countries themselves, and so to mitigate the severity of the attacks. The aim of antimalarial chemotherapy, on the other hand, is to supplement quinine, regardless of cost, with drugs which are effective in those respects in which quinine fails ; that is to say, in preventing infection of man and mosquito, and in preventing relapses. In practical antimalarial work on a large scale, therefore, the question of competition between quinine and the new synthetic drugs does not arise. Some strains of malaria parasites are more virulent than others, and further study of their biological properties is needed ; for example, in many cases of malaria due to *P. ovale* recovery takes place without treatment, because its biological property of virulence is very low. GRASSI recognized two distinct clinical varieties of Italian malignant tertian, a mild and a severe, *mitis* and *immitis*. Again, it required eight

times as much quinine to control the primary attack of cases of malignant tertian malaria infected with the Rome strain, at the Horton hospital, as was required to control cases infected with an Indian strain. In parts of Italy there is need for a better drug than quinine, and atebrin fulfils this purpose. This difference in the resistance of various strains of the same species of parasite greatly increases the difficulty of assessing the value of drugs ; neosalvarsan has a powerful action on the severe Madagascar strain of *P. vivax*, but a very weak action on the mild Dutch strain. Incidentally, plasmoquine with quinine is more effective in preventing recrudescences of this Madagascar strain, than plasmoquine alone. Another complication in drug testing is the degree of immunity which the patient has acquired before treatment. Cases treated at Horton on the first day of the attack, and on each recrudescence, continue to relapse, whatever drug is given ; better results are obtained if treatment is not begun until some tolerance has been acquired. Yet another complication is the natural resistance of the host ; with the same strain of parasite, the attack in one person may be mild, in another very severe. When a person is very susceptible, or the dose of infection very heavy, even so remarkable a drug as atebrin will not cure the case outright. Plasmoquine is a true prophylactic, but the dose required for full protection is too large to be safe ; it is a better preventive of malignant tertian than of benign tertian. Among the ten volunteers at St. Mary's Hospital who were given prophylactic plasmoquine, none had normal primary attacks, but five had primary attacks seven to nine months later (see this *Bulletin*, Vol. 28, p. 973).

Dr. T. A. Henry said that with the view to finding a cheap drug for the cure of malaria the Malaria Commission of the League of Nations had considered the use of the total alkaloids of cinchona. Cinchona febrifuge, in its modern form, was of variable composition and sometimes contained a large proportion of amorphous alkaloids which were stated to be toxic. The Commission finally decided to suggest the preparation of a new cinchona product, to be called "totaquina," which was to be standardized to contain 70 per cent. of the crystallizable alkaloids including 15 per cent. of quinine (this *Bulletin*, Vol. 29, p. 461). In actual practice such a product can be made in two ways. Firstly, the total alkaloids of a suitable cinchona bark may be extracted and precipitated as an almost white powder ; or, secondly, the residues from quinine sulphate manufacture may be brought up to the required standard by the addition of crystallizable alkaloids. All the totaquina so far made on a commercial basis is of the latter type, and is brown in colour. The barks of *Cinchona succirubra* and *C. robusta*, the total alkaloids of which the Malaria Commission had in mind as furnishing the principal supplies of totaquina, are no longer produced anywhere in large quantities, but it is understood that they can be grown over much wider areas than the species providing the rich quinine-yielding barks for which Java is particularly suited. The cinchona industry is now thoroughly rationalized : a perfectly natural step justified by the chaotic condition into which the industry fell some twenty years ago, when far more bark was produced than could be sold at prices which would keep the plantations in being. The dominant position of this rationalized industry is a factor to be taken into account in the production of totaquina. The suggestion that cinchona planting should be revived under Government auspices in the British tropics needs further consideration. Such a revival would merely renew the

old trouble of over-production, and in the long run would benefit nobody. Further, the introduction of synthetic antimalarial drugs may seriously interfere with the demand for quinine, and no one could lightheartedly undertake a large extension of cinchona planting at the present time.

Sir David PRAIN reminded the meeting of the destruction of the indigo and madder industries by the synthetic preparation of indigotine and alizarine, and he said that the existence of the various industries connected with the collection of natural resins and their use in paint and varnish was threatened by the preparation of more satisfactory and permanent varnishes by synthetic methods. The synthetic antimalaria preparations were threatening quinine in the same way, and he agreed with Dr. Henry that the time had come when it was no longer fair or justifiable to urge the extension of cinchona planting.

Professor SWELLENGREBEL spoke of the different degrees of resistance to drugs found among strains of the same species of malaria parasite. He was forced to conclude that JAMES's Madagascar strain of benign tertian was exceptionally refractory to treatment with plasmoquine and quinine, because a large proportion of his own cases infected with this strain relapsed, while PIEBENGA treated 67 cases infected with a native Dutch strain and none relapsed. He considered that a system of prophylaxis and treatment, which was of proved value, might break down under the stress of an unusual number of infective bites or the prevalence of a strain of parasites with a high degree of vitality.

Dr. NICOL reported on the results of the treatment of 161 mosquito-infected cases of benign tertian at Horton. Among them were 21 latent cases in which the primary attack occurred after an incubation of 25 to 40 weeks. Eighty-one of the patients relapsed, but none relapsed later than 12 months after the primary attack. Long relapses or recurrences are not the result of weather conditions : the return of fever is entirely dependent on the date of the original infection. Irrespective of the season of the year, the long recurrences show an interval of seven to nine months from the primary attack, just as the latent cases show an incubation period of the same duration.

Dr. P. MANSON-BAHR reported that in four cases of subtertian malaria from West Africa, schizonts disappeared after 0·9 gram of atebrin had been given, and there were no toxic symptoms. The drug did not appear to have such a powerful action in benign tertian.

Sir Malcolm WATSON said that on a mine which he visited in Africa the medical officers were disappointed with atebrin, and were fully satisfied that it was slower in action than quinine. Possibly the strains were exceptionally resistant.

Professor SCHULEMANN of Elberfield stated that quino-plasmoquine which is plasmoquine combined with quinine in the proportion of 1 to 30, is able to reduce the relapse rate in benign tertian from the usual 50 per cent. to about 3 per cent. : but there are certain resistant strains, such as James's Madagascar strain, where this treatment fails to reduce the number of relapses. In quartan malaria, in actual practice, no relapses have been noted with plasmoquine treatment ; but in subtertian malaria the percentage of relapses is not reduced. It is of great importance that comparative investigations should be made to determine whether a particular strain of parasite occurring in a native in the tropics, shows the same susceptibility to drugs as it does in a European in the temperate zone. A large number of different

species of plasmodia occurring in birds was examined by Dr. KIKUTH who was not able to find any difference in their susceptibility to drugs. It was not until he investigated paddy birds infected with *Haemoproteus orizivorae* that any advance was made. In these, it was found that plasmoquine caused the gametocytes to disappear from the blood, but they soon appeared again when the drug was stopped, because they developed from the schizonts lying in the endothelial tissues of the internal organs, where the drug had been unable to reach them. When atebrin was given with the plasmoquine, the schizonts were destroyed and the relapses were stopped. JAMES's work has shown that in tests on birds it was necessary to transmit the infection by means of mosquitoes, and tests are now being made on those lines.

Sir Aldo CASTELLANI said that in his experience plasmoquinine was a less potent drug than quinine, and that in exceptional instances it might start an attack of blackwater. *W. F.*

ORENSTEIN (A. J.). **Atebrin in the Treatment of Severe Malaria.**—*Brit. Med. Jl.* 1932. July 2. pp. 8–10. With 8 charts in text.

Eight cases of malignant tertian, some of them complicated by an additional infection with benign tertian, were given one decigram of atebrin and one centigram of plasmoquine three times a day for four successive days, the course being repeated after a few days. No unpleasant symptoms due to atebrin were observed (there was slight scleral jaundice in two cases), but in three patients there were cramps and headache ascribed to plasmoquine. All the cases were severe, and one was eight months pregnant. The results were excellent.

W. F.

DE MELLO (Froilano) & DE AZEVEDO (Antonio). Note préliminaire sur l'action plasmodicide de l'atébrine. [**The Plasmodicidal Action of Atebrin.**]—*Bull. Soc. Path. Exot.* 1932. Oct. 12. Vol. 25. No. 8. pp. 874–878.

——, BRAS DE SA (L. J.) & DE AZEVEDO (Antonio). Résumé des observations concernant l'action plasmodicide de l'atébrine.—*Ibid.* pp. 878–881.

The authors received from Dr. WICHS of Calcutta a supply of 0·2 gram tablets issued from the Bayer-Meister Lucius laboratories as Erion or Plasmochine E, the names which were first given to atebrin. Different species of animals tolerate atebrin in different degrees. Cats tolerate 0·05 gram per kilo, but they are killed by 0·1 gram per kilo, though rabbits show no toxic symptoms after this dose. When fatal doses have been given there is fatty degeneration in the liver and kidneys. [For preliminary tests in the malaria of birds, see KIKUTH, this *Bulletin*, Vol. 29, p. 705.] The authors treated 3 cases of benign tertian, 3 cases of quartan, 6 cases of subtertian, and 6 cases of mixed infection. The drug acted well in every case ; all parasites disappeared under its influence, except the crescents of subtertian, and there were no relapses during periods of observation lasting 1 to 4 months. They conclude that atebrin with plasmoquinine will be at least as good as quinine with plasmoquine for use in malarious countries. *W. F.*

Eckhardt (A.). Ueber die ambulante Behandlung der Malaria tropica mit Atebrin bei Negerkindern in Afrika. [**Ambulatory Treatment with Atebrin of Negro Children in Africa.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Oct. Vol. 36. No. 10. pp. 521–530.

The results are given in four tables. The first shows treatment with atebrin alone, the second and third with atebrin and plasmoquine, the fourth with intramuscular injections of atebrin. He concludes that atebrin has proved very useful in the ambulatory treatment of malignant tertian malaria in 116 negro children. It has an excellent action on the schizonts, but none on the gametocytes. In 4 to 5 days the drug produces both a clinical and a parasitological cure. The short period of treatment required is one of the greatest advantages of atebrin. No toxic effects were noted and it exerted a beneficial action on the general health. No yellow discoloration or photosensitiveness of the skin was noted. The dosage for the children, in grams, was as follows:—

Age.	Daily dose.	Total amount.
0–½ year	0·025	0·075–0·1
½–1 ,,	0·05	0·15–0·2
1–2 years	0·1	0·3–0·4
2–4 ,,	0·15–0·2	0·45–0·6
4–8 ,,	0·3	0·9–1·0
Half grown	0·3	1·2–1·5

E. D. W. Greig.

Kikuth (W.). Atebrin: ein neues synthetisches Malariaheilmittel. [**Atebrin; a New Antimalarial Synthetic Drug.**]—*Riv. di Malariologia.* 1932. Mar.–Apr. Vol. 11. No. 2. pp. 157–164.

——. I risultati finora ottenuti in clinica col nuovo antimalarico sintetico "Atebrin."—*Ibid.* No. 3. 13 pp. [11 refs.]

This paper is itself a review of all the records of note up to the present of the use of atebrin in malaria and cannot, therefore, be satisfactorily abstracted. The work of Sioli, Peter, Mühlens, Fischer, James, Nicol and Shute, Green, Napier and Das Gupta, Strickland and Roy among others is referred to and these have already been noted in this *Bulletin*, 1932, Vol. 29, No. 10, pp. 695 & 705 *et seq.*). The author quotes Mühlens and Fischer that "in benign tertian malaria atebrin has an action on the schizonts at least equal to that of quinine," and he states that all investigators are agreed that "in subtertian malaria atebrin exerts a specific action on the schizonts of *P. falciparum*, but has no effect on the gametocytes" and it acts best, therefore, in conjunction with plasmoquine. The beneficial results in young children with high fever and grave general state are stressed.

A further great advantage being that the course of treatment, 4 days or so, is, though short, effectual.

The use of atebrin in blackwater fever is dwelt on [*tom. cit.*, p. 706] and the comparative absence of signs of intolerance—severe headache (in 2 out of 50 patients treated by Green in Kuala Lumpur and 4 with digestive disturbance). The experiment in prophylaxis by Napier and Das Gupta (*tom. cit.*, pp. 707 & 709) is quoted. In short, this article is an excellent review of our present knowledge with regard to atebrin. *H. H. S.*

JARVIS (O. D.). **Results of Treatment of Malaria by (*a*) Plasmoquine and Quinine, and (*b*) Atebrin, together with Some Observations on Malaria Convalescents.**—*Jl. Roy. Army Med. Corps.* 1932. Sept. & Oct. Vol. 59. Nos. 3 & 4. pp. 190–199; 252–262. With 5 figs.

Cases of relapsing benign tertian malaria to the number of 126 were treated with daily doses of 0·03 gram plasmoquine and 20 grains of quinine for three weeks, with the result that only 6 cases relapsed during the period of observation, which lasted for 12 weeks. Five cases were treated with atebrin, 0·1 gram daily, for seven days. There were no relapses. Atebrin was present in the urine, on an average for 26 days after the conclusion of treatment. In one case it appeared on the second day of treatment and was present for 37 days. (See United Fruit Company's report above.) *W. F.*

MORISHITA (Kaoru), MIYAHARA (Hatsuo) & ISHIOKA (Hiozo). **Studies in the Treatment of Malaria. VII. Experimental Treatment with Plasmoquine (II Report). Effect of 10 days' or 2 Weeks' Treatment in Benign and Malignant Tertian Malaria. VIII. Experimental Treatment with Plasmoquine (III Report). Behaviour of Quartan Malaria towards our 5 Days' Treatment with Plasmoquine and Quinine. IX. On the Therapeutic Value of the Modified Taiwan Method in Various Forms of Malaria.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1932. July. Vol. 31. No. 7 (328); Sept. No. 9 (330). [In Japanese. English summaries pp. 70–73; 75–76; 88–91.]

The daily dose was 0·06 gram plasmoquine, with or without 0·75 gram quinine sulphate. The period of observation subsequent to treatment was eight weeks. After one week's treatment, the relapse rates were: benign tertian 14 per cent., malignant tertian 43 per cent., quartan no relapses.

Eleven cases of quartan malaria were treated with the smaller daily dose of 0·04 gram plasmoquine and 0·8 gram of quinine sulphate for five days. None of them relapsed but 2 control cases on quinine both relapsed. [See SCHULEMANN, above.]

Anti-malaria measures in Formosa, owing to the configuration of the country, are almost limited to the administration of quinine. Every year some 40,000 persons are treated at public expense. The authors found that though the clinical features were much improved, the method was a failure as regards protection, for 67 per cent. of the benign tertian cases relapsed within 8 weeks. *W. F.*

REED (J. G.). **Note on the Passage of Plasmoquine Compound Tablets in the Stools.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1932. June 30. Vol. 26. No. 1. pp. 95–96.

Two Tamil women who were taking 3 tablets of plasmoquine compound daily, were treated for worms; one was given santonin, the other chenopodium. In the first case, when the stools were searched for worms, several broken tablets of plasmoquine were seen. In the second case, six tablets were recovered almost unchanged from the stools, and as none had been given on the day of the chenopodium treatment, some must have remained in the body for at least 48 hours. *W. F.*

Gorodezky (A. S.) & Fastowskaja (E. I.). Ueber die Behandlung der Malaria mit Plasmochin. [**Treatment of Malaria with Plasmoquine.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Nov. Vol. 36. No. 11. pp. 568–576.

The authors working on practical lines in Artemowka (Don valley) desired to explore more fully than had been already done the uses of plasmoquine. They treated 198 malaria cases, of which *Plasmodium vivax* was found in 142, *Plasmodium praecox* in 15, *Plasmodium malariae* in 2, mixed infection 1 ; parasites were not found in 38 cases. The scheme of treatment was that recommended by Mühlens, 1st week 7 days' treatment, 2nd week 4 days' interval 3 days' treatment, 3rd to 6th weeks as in 2nd week. The doses for adults were 3 tablets of 0·02 gm. plasmoquine thrice daily; for children the dose was proportionately smaller. 124 persons were treated with plasmoquine alone, 71 with plasmoquine compound and 3 with plasmoquine and plasmoquine compound. They conclude from their investigations that the chief advantage of plasmoquine over quinine is from the epidemiological point of view, causing as it does the rapid disappearance of the sexual forms from the peripheral blood. It is quite feasible to employ plasmoquine in ambulatory cases. The capacity for work is more rapidly restored by plasmoquine than by quinine. Another advantage over quinine is that it is tasteless, In children the doses employed were relatively too high and cyanosis was frequently noted. They were unable to correlate the frequency of relapses with the duration of treatment. *E. D. W. Greig.*

Miyahara (Hatsuo) & Ishioka (Hyozo). **Observations on the Velocity and Duration of the Quinine Excretion in the Urine of Malaria Patients.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1932. Sept. Vol. 31. No. 9 (330). [In Japanese. English summary pp. 87–88.]

The velocity of excretion was measured by the time elapsing between the administration of quinine and its appearance in the urine ; the duration was measured by the time between administration and the last time when quinine could be detected in the urine. The kind of quinine salt used, and its solubility, made little difference in the velocity and duration of excretion. When quinine was taken on an empty stomach, it appeared more quickly in the urine than if taken after a meal, but the duration of excretion was the same. Magnesium sulphate lowered the velocity of excretion. The smaller the quantity of the drug the lower was the velocity and the shorter the duration. The velocity was very high after intravenous injection and the duration relatively long. *W. F.*

Ottolenghi (Donato). Untersuchungen ueber die medikamentöse Prophylaxe der Malaria. [**Drug Prophylaxis of Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Dec. Vol. 36. No. 12. pp. 623–637. With 2 figs. [17 refs.]

In the year 1931 the author commenced a program in Italy to test the value of what he describes as therapeutic sanitation (bonifica umana). For the purpose he selected two districts, one near Ferrara the other near Ravenna. At Ferrara the drugs employed were :—(1) Baccelli mixture (each tablet containing quinine hydrochloride 20·00 cgm., iron citrate 0·25 cgm., sodium arsenate, 0·05 cgm. ; for

children under 10 years the quantity was reduced). The treatment was administered for 2 periods of 3 weeks in May and June with an interval of 10 days. Adults were given 2 tablets in 1st week, in 2nd 3, in 3rd 4. Children under 5 received quinine tannate in chocolate. (2) Quinoplasmoquine (tablets of 1 cgm. plasmoquine, 30 cgm. quinine sulphate). Children under 10 quarter dose. For children under 5 it was given in syrup. It was administered in 2 periods of 10 days each with an interval of 1 month. First period, 1st and 2nd days 3 tablets, 3rd day 2, 4th to 10th day 1. Second period 1st and 2nd days 2, 3rd to 10th, 2. The following table gives the results of the observations at Ferrara on the total population treated (385) up to the end of November :—

Malaria cases in population in percentages.

Treatment	With antilarval measures		Without antilarval measures	
	Reduction	%	Reduction	%
Baccelli mixture	6·4 (49·7)	87	13·0 (56·5)	76
Quinoplasmoquine ...	7·8 (68·9)	88	7·1 (53·4)	82
Untreated	12·9 (49·1)	73	16·8 (36·8)	54

Figs. in brackets represent the malarial cases in same population groups in 1930.

At Ravenna 4 zones were chosen and only quinoplasmoquine was administered in the same doses, as in first experiment. Two periods of 10 days treatment with an interval of 5 to 10 days. The results at Ravenna are shown in the 2 following tables :—

Place	Popu-lation	Persons treated	Total number malarial cases in summer				Treat. started
			Te	Tr	Pr		
Chiavica Romea ...	600	81	1	—	—		End of May
Control zone ...	345	—	38	—	—		—
Mandriole	582	274	10	—	5	(Te)	Mid June
Primaro	208		2	9	3	(Tr)	
Control zone ...	302	—	43	—	13		—
Fosso Ghiaia ...	368	131	5	—	3		End of May
Control zone ...	111	—	30	—	8		—

Course of malaria in ascertained parasite carriers.

Place	Treated persons	Before			After first treat.			After second treat.			In Oct.			In Mar. & Apr.		
		M	Te	Tr	M	Te	Tr	M	Te	Tr	M	Te	Tr	M	Te	Tr
Mandriole Primaro	274	126	21	14	118	7	4	89	0	2	86	0	0	34	4	0
Fosso Ghiaia	118*	47	9	–	46	7	–	32	0	–	31	0	–	7	1	–

M=splenic enlargement ; Te=benign tertian ; Tr=malignant tertian ; Pr=primary infection. * 13 more cases treated with quinine tannate.

The author concludes that his experiments and practical observations are of great value for drug prophylaxis, on the basis of quinine and plasmoquine, if they are carried out on the correct lines as laid down in this and other publications. *E. D. W. Greig.*

STOUTE (D. G.). **Clinical Observations on Malaria treated with Tebetren.**—*Lancet.* 1932. Sept. 10. pp. 565–566.

Tebetren is methyl-hydrocupreine-methyl-acridine-dehydrocholate, in which quinine is combined with an acridine dye and united with a bile-salt to render it non-toxic. It was supplied to the author in three-grain tablets and in ampoules. Subcutaneous injections caused sloughing, but intramuscular injections produced no reactions. Routine treatment was oral, and consisted of two tablets every 4 hours, until 60 had been taken. Four such courses were given with an interval of 3–5 days between the courses. The author treated in Zululand some 80 European adults and about 20 children. He concluded from the results that the action of tebetren was even more rapid than that of quinine, and little or no toxic symptoms appeared beyond a fullness of the head, with deafness, and singing in the ears. Fourteen patients who protected themselves from re-infection by screening their quarters had not relapsed during a period of 18 months following treatment. *W. F.*

SERGENT (Et.), SERGENT (A.), TRENSZ (F.) & VOGT (D.). Essais de traitement du paludisme à *Plasmodium praecox* par le 710 Fourneau, seul ou associé à la quinine, chez des paludéens d'Algérie. [**Fourneau 710 in the Treatment of Malignant Tertian.**] —*Arch. Inst. Pasteur d'Algérie.* 1932. Mar. Vol. 10. No. 1. pp. 1–21. With 5 figs.

Fourneau and his colleagues have studied the action of a product bearing the number 710 ; like plasmoquine, it is a quinoline derivative ; it has a chain of three carbon atoms, and its molecular weight is 286. It is a yellow powder, soluble in water. They concluded from a study of its action on *Haemoproteus orizivorae* that it could be substituted for plasmoquine with advantage, because it was less toxic and could be produced at a lower cost. MONIER [this *Bulletin*, Vol. 28, p. 1012] treated with the drug 2 paralytics therapeutically infected with *P. vivax*, 2 cases of chronic infection with *P. vivax*, and one chronic infection with *P. falciparum*. The parasites disappeared in all four benign tertian cases ; but one of the naturally infected patients relapsed ten days later. The drug had no apparent effect in the malignant tertian case.

The authors treated 20 cases of subtertian ; 19 were chronic infections in natives, one was a first attack in a European. The doses given were 0·04 gram on the first day, 0·06 gram on the second, and 0·08 gram on the third and following days. A course lasted from 5 to 9 days, and was repeated several times in many of the cases. Eleven cases were treated with 710 alone, and nine with 710 associated with quinine. It proved very toxic, 12 of the 20 patients showed signs of intolerance—asthenia and muscular fatigue, headache, severe abdominal pain, and vomiting. These symptoms disappeared when adrenalin was administered. It had no action on the schizonts of *P. falciparum* ;

crescents were present in only two cases, they disappeared in two to four days. It was difficult to assess the value of 710 in those cases where it was given mixed with quinine. *W. F.*

Sur (S. N.), Sarkar (H. P.) & Banerji (K. M.). **Plasmochin as a Malarial Gametocide.**—*Indian Med. Gaz.* 1932. Sept. Vol. 67. No. 9. pp. 490–493.

Anopheles were fed on malaria patients, and kept for dissection. The patients were then given 0·02 gram plasmoquine for 3 days. On the eighth day, a blood examination was made and a second lot of mosquitoes was fed on the patients. These comprised 17 cases of malignant tertian, 17 of benign tertian and 9 quartan. As a result, out of 679 mosquitoes which had fed before plasmoquine was given 16 per cent. were found infected when they were dissected 12–15 days later ; but, out of 456 mosquitoes which fed after plasmoquine treatment, none became infected. The mosquitoes employed in this experiment were *A. fulginosus*, *A. varuna*, *A. stephensi*, *A. ludlowii*, *A. maculatus* and *A. willmori*. [It is interesting to note that 13 per cent. of the mosquitoes fed on untreated quartan cases became infected.]

W. F.

Sergent (Et.) & Catanei (A.). Essai de traitement du paludisme des oiseaux (*Plasmodium relictum*) par l'ichthargan. [**Ichthargan in Bird Malaria.**]—*Arch. Inst. Pasteur d'Algérie.* 1932. Mar. Vol. 10. No. 1. pp. 37–38.

The authors administered the drug to canaries infected with *Plasmodium relictum*, but it had no effect upon the parasites. *W. F.*

Winfield (G. A.). **A Study of the White and Differential Counts in Six Unselected Cases of Inoculation Malaria.**—*Jl. Lab. & Clin. Med.* 1932. July. Vol. 17. No. 10. pp. 985–992. With 6 charts. [24 refs.]

Six cases of inoculated benign tertian malaria were examined. Only two were treated with quinine. Leucopenia was present, with a gradual return to normal after recovery. Neutrophiles fell gradually and showed a marked fall at the termination of the infection ; lymphocytes, on the contrary, showed a slight rise throughout the course with a sharp rise at the termination. Monocytes showed a moderate rise. The Arneth count is of value because the immature, non-filamented neutrophiles are increased in proportion to the severity of the attack.

W. F.

Mayne (Bruce). **Note on Experimental Infection of *Anopheles punctipennis* with Quartan Malaria.**—*Public Health Rep.* 1932. Aug. 26. Vol. 47. No. 35. pp. 1771–1773.

The therapeutic inoculation of benign tertian malaria is useless in the case of negroes, because they are almost completely refractory ; but, as they develop severe attacks of malaria after direct blood inoculation with quartan malaria, it became important to infect anopheles with *P. malariae*. Anopheles (157 *A. punctipennis*, 39 *A. quadrimaculatus*, and 7 *A. crucians*) were fed on three patients suffering from quartan malaria with the result that six *A. punctipennis* became infected. Gland infection was found in only one, and it was scanty.

W. F.

TALIAFERRO (William H.). **Experimental Studies on the Malaria of Monkeys.**—*Amer. Jl. Hyg.* 1932. Sept. Vol. 16. No. 2. pp. 429–449. With 1 fig. [51 refs.]

This work was done with *Plasmodium brazilianum*, a quartan-like parasite of Panama monkeys. The immunity which develops during infection is due to the stimulation of the macrophages, especially in the spleen and liver, For the first 48 hours after the injection of a large dose, parasites occur in the sinusoids of the spleen and liver without evidence of phagocytosis or stimulation. At the time of the crisis, the parasites become concentrated in these organs ; but after a day or two of this concentrating process, the macrophages suddenly become very active and destroy them. The splenic follicles swell to several times their normal size, numerous active macrophages appear in the follicles and the Kupffer cells enlarge. This heightened phagocytic activity is specific, and is probably due to opsonization of the parasites by a specific antibody. The author thinks it probable that relapses are due to temporary cessation of macrophage activity. *W. F.*

WARASI (W.). Zur Biologie des Malariaparasiten. [**Biology of the Malarial Parasite.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Aug. Vol. 36. No. 8. pp. 425–429. With 1 text fig. [17 refs.]

It was noted that haemoglobin was never present in the vacuole of the parasite, although the plasmodium has no visible membrane. However when it enters a red cell the parasite becomes enveloped in a membrane, derived from the red cell, which has special properties. He considers that this observation explains why the young parasites have no haemoglobin in the vacuole and enables him to reaffirm that the malarial pigment is a special substance related to melanin ; further it partially explains the action of quinine on the parasite, because the membrane not only isolates the parasite from haemoglobin but also from quinine, the latter being also adsorbed by the former. Therefore quinine has no action on the intracellular parasites, only on the extracellular forms. *E. D. W. Greig.*

OTERO (F. Quintana). Malaria und Blutzuckerkonzentration. [**Malaria and Blood Sugar Concentration.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Sept. Vol. 36. No. 9. pp. 461–473. [46 refs.]

The author reviews the literature of the subject and then records his own observations. In a table he sets forth his blood sugar estimations in 100 cases of benign tertian malaria. In 44 of these he estimated the sugar both before and after treatment with quinine. As a result of his research he concludes that :—Glycaemia was present in 84 per cent. of the malarial cases observed. The rise of the blood sugar has no relation to the attacks ; it may occur either during an attack or in a fever-free interval. The alkali reserve diminishes more during an attack than in a fever-free interval ; the average value in both periods was 48·7. At first the hyperglycaemia is a reaction to the parasite, but later it is almost always caused by lesions of the liver cells. The disturbances observed were all of a temporary character and disappeared with treatment. *E. D. W. Greig.*

Chorine (V.). Un nouveau traitement du sang en gouttes épaisses pour la recherche des parasites du paludisme. [**A New Method of staining Thick Films for Malarial Parasites.**]—*Bull. Soc. Path. Exot.* 1932. June 8. Vol. 25. No. 6. pp. 561–563.

Dry at a low temperature. Fix in 10 per cent. commercial formalin until dehaemoglobinization is complete, 3 to 15 minutes. Wash. Treat with a solution consisting of 3 cc. of Lugol in 100 cc. of a 2 per cent. solution of potassium iodide, for 3 to 5 minutes. Rinse. Treat with 0·5 per cent. sodium hyposulphite, for 3 to 5 minutes. Wash. Stain in Giemsa, 2 drops to each 1 cc. of hard tap-water, for 1 hour. The formalin dehaemoglobinizes and fixes at the same time. It is advisible to add calcium carbonate to the formalin, to neutralize acidity. The optimum pH is 7·3 to 7·5 [see Green, this *Bulletin*, Vol. 29, p. 718]. *W. F.*

Kopeloff (Nicholas), Blackman (N.) & McGinn (B.). **"Asexualization" of the Plasmodium in Induced Malaria.**—*Amer. Jl. Med. Sci.* 1932. Aug. Vol. 184. No. 2. pp. 262–265.

A strain of malaria, known as the Poughkeepsie strain, has been employed for the treatment of paralytics in New York since August 1929. Transmission has been effected by inoculation of blood. Blood-films from at least one patient at each passage have been examined daily. During this time, the proportion of patients with gametocytes became gradually less, and since October 1930 no gametocytes have been found in any of the films examined. A second strain, known as Institute strain, which has been in therapeutic use since 1923, has long since ceased to produce sexual forms. [The absence of gametocytes was determined by the examination of films only; attempts to transmit by anopheles were not made.] *W. F.*

Breindl (V.) & Jirovec (O.). **Einige Bemerkungen ueber die Nuklealreaktion bei** *Laverania malariae* **und** *Proteosoma praecox.* [**Observations on the Nuclear Reaction in** *Laverania malariae* **and** *Proteosoma praecox.*]—*Zent. f. Bakt.* I. Abt. Orig. 1932. Nov. 17. Vol. 126. No. 3/4. pp. 184–186. With 3 figs.

Sections from the organs of a fatal case of malignant tertian malaria in the Tropical Diseases Hospital, Hamburg, more particularly the brain, were stained by the Feulgen method, which is a specific stain for nuclear chromatin. Sections were also made of the intestine of culex infected with proteosoma and stained in the same manner. From their investigations the authors conclude that in the dividing forms of *P. falciparum* in the capillaries of the brain as well as in sporocysts and sporozoits of *Proteosoma praecox* in the intestine of culex, a positive nuclear reaction of nuclear chromatin takes place. Contrary to the view of Pawan [this *Bulletin*, Vol. 28, p. 1025] the nuclei of the malaria parasite and of bird malaria have the same chemical structure as other protozoa. That the reaction is apparently negative in rings and gametocytes is not surprising having regard to the very small amount of chromatin and the smallness of the nuclei in the rings and the diffuse division chromatin in the gametocytes. *E. D. W. Greig.*

Wakeshima (Takashi). **Studies on Acid-Alcali-Equivalence in Malaria. I. The CO_2 Content in the Blood-Plasma.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1932. Aug. Vol. 31. No. 8 (329). [In Japanese. English summary pp. 81–82.]

In almost all cases there is a diminution in the alkali reserve and "acidosis," especially during the attack. The average CO_2 content in

13 healthy Formosan Chinese was 56·3 per cent. In malaria patients, it was about 6 per cent. lower. Even 8 weeks after cessation of treatment the normal level had not been reached. *W. F.*

KAPPUS (A.). Ueber die Henry'sche Malariareaktion. [**Henry's Malaria Reaction.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Nov. Vol. 36. No. 11. pp. 576–586.

At the 2nd International malaria conference at Algiers in May 1930 HENRY communicated his method of serological diagnosis of malaria, which he had published a few years previously. The method was tried out by the author in the Tropical Diseases Hospital at Hamburg. As it was practically impossible to get true malarial pigment in sufficient quantity for his purposes HENRY employed as antigens iron albuminate and a melanin. The author employed 2 tests, a ferroflocculation and a melanoflocculation. The antigen of the first is a ferrum albuminate (Merck) No. 113 in stock solution of 1–600, for the second he used the choroid of the eyes of freshly slaughtered oxen. He gives full details for carrying out the tests. He investigated 143 sera obtained from 83 different persons. These included malarial cases and controls ; of the former there were 34 cases in which plasmodia had been found in the blood, of which 24 were malignant tertian, 8 benign tertian and 2 mixed infections of these two. As a result of his investigations the author concludes that almost all the positive reactions occurred with sera from malaria cases ; occasionally non-specific reactions occurred correlated with alterations in the serum, *e.g.*, jaundice, pyrexial therapy, etc. He considers the test a valuable help for the diagnosis of malaria, but he is unable to express an opinion as to its value in gauging the therapeutic effects of malarial treatment. *E. D. W. Greig.*

RAMSAY (G. C.) & SAVAGE (J. de la M.). **The Principles and Methods of Malaria Control in Assam.**—*Brit. Med. Jl.* 1932. Oct. 29. pp. 790–792.

A. minimus is the carrier of malaria in Assam. It breeds in clear water and can be found at the grassy edges of streams with a moderate current, for its well-developed tail hooks enable it to hold on ; it is also found in clear stagnant water. It selects places exposed, or partially exposed, to sunshine. It does not breed under dense shade, or in water which is contaminated or contains silt. The heavy monsoon rainfall makes most swamps undrainable. Those that are cultivated cannot be oiled because oil would spoil the crops. These should be dusted with Paris green, and those which are uncultivated should be allowed to grow up in shade. The irrigation channels in the high-lying, terraced rice-fields are intensely malariogenic. Periodic drying by controlled irrigation, or the cultivation of crops which do not require it, is the remedy. Subsoil drainage is too costly and, in most places, it is impracticable, owing to the high level of the subsoil water. The most efficient drainage is by concrete inverts ; but the drains must have a grade of at least 1 in 200, for slow-running drains are intensely malariogenic. For this reason borrow-pits containing clear water should not be connected up with the object of draining them ; the impervious pan at the bottom should be broken to assist percolation, and the water should be contaminated by filling in with soil, refuse from the coolie-lines, or cut jungle. Fish, water-beetles, and other natural enemies of mosquito larvae are all very well in the laboratory,

but they are of little use in the field. "Former popular beliefs that dirty water and dense virgin jungle . . . were the sources of malaria in Assam, have been shown to be erroneous, as also the idea that the pioneer who clears or drains is necessarily benefiting mankind. . . . The anopheline mosquito, which transmits our malaria, does not breed under dense shade, or in water which appears to be noisome or revolting. . . In future the control of malaria in Assam will mean less interference with nature and a realization of the fact that the green beauty of vegetation covering rivers, streams, and swamps can be allowed to remain with improved health to mankind." The shade should be dense if it is to prevent breeding; a practical test is that it should be thick enough to prevent grass growing beneath it. *W. F.*

Wallace (R. B.). **Cessation of Oiling in a Malarious Area during a Certain Season of the Year.**—*Malayan Med. Jl.* 1932. Sept. Vol. 7. No. 3. pp. 73–81. With 7 charts.

Observations made during a period of 6 years, on a group of rubber estates, demonstrated that malaria had a seasonal incidence in the Malay States, and the author found that during the healthy season, from the middle of October to January, oiling could be suspended with impunity, and with the saving of hundreds of pounds. (See Report of Malaria Advisory Board above and Vol. 28, p. 609.) *W. F.*

Corner (J. D.). **The Employment of the Portable Pump in Anti-Malaria Schemes.**—*Jl. Roy. Army Med. Corps.* 1932. Aug. Vol. 59. No. 2. pp. 138–141. With 3 figs.

In the station, Kamptee, India, one of the greatest handicaps encountered in anti-malaria schemes is the maintenance of effective drainage of monsoon and post-monsoon rain-water which supplies the chief temporary breeding areas. The nature of the ground—loose, sandy cotton soil—precluded effective drainage since the sides of any kutcha drain fell in almost immediately after it had been opened up. A fresh problem presented itself this year in the shape of drainage of water from excavations in solid rock. Oiling was unsatisfactory and expensive, and the author, with no available funds for effective drainage solved the problem satisfactorily by the purchase of two small hand-worked rotary pumps at Rs.25 each. [Size and delivery not given.]

The water could be dealt with—(1) By pumping and spraying widely over the ground; (2) by pumping into neighbouring drains; (3) by pumping into buckets, carried by coolies to the drains; (4) by pumping small collections of water into one large central pool which could be heavily oiled pending disposal of its contents. [In similar circumstances where, however, larger funds are available, a small portable petrol-driven rotary pump will be found to be efficient and economical and will throw to greater heights.] *H. Home.*

Swellengrebel (N. H.) & de Buck (A.). **Plasmoquine Prophylaxis in Benign Tertian Malaria.**—Reprinted from *Proc. Roy. Acad. Sci. Amsterdam.* 1932. Vol. 35. No. 6. pp. 911–914. With 1 graph.

The authors have reported already (see this *Bulletin*, Vol. 29, p. 357) their attempt to prevent malaria by giving 0·03 grams of plasmoquine

daily, beginning on the evening preceding the infecting bites, and continuing for six days. These attempts were unsuccessful except in the one case with which this paper is concerned. After being bitten by infected mosquitoes in September, this man remained in good health until the following April, when he had his first attack of benign tertian fever, 7 months and 18 days after the infecting bites. [See also JAMES in this number.] The remittent character of the fever showed that it was not a relapse following a slight unnoticed attack soon after the bites, but that it was the initial fever which is encountered only in subjects suffering from malaria for the first time in their lives. The infecting strain in this experiment was James's Madagascar strain, and each volunteer was bitten by several mosquitoes. The number of relapses which occurred in the other subjects of the experiment in spite of treatment, the high infection rate by means of mosquitoes, and the short incubation period, showed that this strain possessed an exceptionally high vitality—higher for instance than the strains native to Holland—and it may be that this high vitality, combined with the large number of bites inflicted, was the cause of failure to protect with plasmoquine. The authors conclude that their failure to prevent the primary attack and the relapses cannot be regarded as contradictory to statements announcing satisfactory results elsewhere, but that it shows that a system of proved value in prophylaxis and treatment may break down under the stress of an unusually great number of infected mosquitoes or the prevalence of some strain of parasites of particular vitality. *W. F.*

SERGENT (Edmond) & SERGENT (Etienne). Le péril paludéen à l'armée d'Orient. [**The Malaria Peril of the Army on the Eastern Front.**]—*Arch. Inst. Pasteur d'Algérie.* 1932. Sept. Vol. 10. No. 3. pp. 317–336. With 5 diagrams & 1 map. [17 refs.]

This story tells how the French Army in Macedonia was held up by malaria during the war, and how the danger was overcome by the proper use of quinine. The army disembarked at Salonika in the autumn of 1915. ROSS, LAVERAN and others gave clear warning, in January and February of 1916, that severe malaria would be experienced unless timely precautions were taken ; but although plans were made and orders were issued, the ignorance of the officers, of the common soldiers, and even of the doctors, prevented their proper execution. The authorities charged with the application of prophylactic measures, mocked and laughed at them ; were they not the dreams of doctors haunted by an *idée fixe*? One hospital where proper precautions were taken, and which was properly screened, was regarded with ironical contempt. Perhaps more important than all, the medical officers did not know how to give quinine, and they did not believe in it. The result was disaster. In 1916 there were some 60,000 cases of malaria, in a force of about 115,000 men. In the autumn, there were not more than 20,000 men in the line. General SARRAIL reported to the government that his army was immobilized in hospital. In January 1917 the authors were sent out to investigate and to draw up a plan of action. They decided that antilarval measures on a large scale were not expedient for the protection of an army in temporary occupation of a country, and they recommended quinine prophylaxis rigorously applied. Minute details were given as to the way it was to be given under personal supervision ; everyone was to take quinine every day, not as

a medicine but as a ration ; refusal to take it was to be regarded as a refusal to obey orders in the face of the enemy. [The quinine was in tablet form.] A special antimalaria service was created, whose chief duty was to see, by testing the urine with Tanret's reagent, that quinine was being properly given in the different units. The responsible officer was punished, not the private soldier, when the tests were unsatisfactory. Vigorous propaganda was carried out.

The result was success, and the army was saved. A chart shows that whereas in 1916 the malarial peak, in September, was reached with

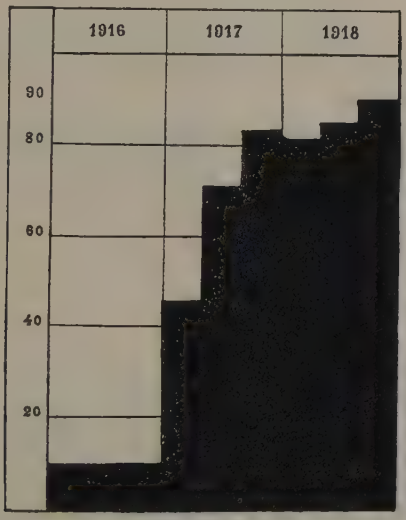


Diagramme 2

Diagram illustrating the efficacy of chemical control of quininisation in the French Army in Macedonia. The number of men found by Tanret's reaction to be properly, taking their daily prophylactic dose of quinine was under 15 per cent. in 1916 as against nearly 100 per cent. in 1918.

[Reproduced from *Archives de l'Institut Pasteur d'Algérie*]

8,000 primary cases (4 divisions), in 1917 with 8 divisions the peak did not exceed 1,000 primary cases. In 1916, there were 379 deaths from malaria; in 1917, 71 ; in 1918, 54. Tanret's reaction showed that only about 15 per cent. of the men were taking their quinine in 1916, but by 1918 nearly 100 per cent. were taking it. The German army, on the same front, which had no special antimalaria organization, served as a control, and they had much more malaria in 1917 than in 1916. *W. F.*

DE ALDA (Martin). Nota sobre las recidivas observadas en los enfermos de paludismo. [**Relapses in Malaria Patients.**]—*Medicina Países Cálidos.* Madrid. 1932. Nov. Vol. 5. No. 6. pp. 511–513.

Having noted an exceptionally large proportion of relapses in malaria patients at Arcos de la Frontera (Cadiz) during the first four months of 1932, the author investigated the question of cause, studying the figures of the preceding two years. He found that in 1930 the method of treatment was to give 40 gm. of quinine [? which salt] over 55 days,

namely 15 gm. in the first 15 days, then 1 gm. on alternate days for 30 days and 10 gm. the last 10 days. That year the percentage of relapses was 2·1.

In 1931 a total of 25 gm. in 40 days was given : 10 gm. during the first 10 days and 1 gm. every other day during the next 30 days. The relapse percentage rose to 8·7. In 1932 the routine was to give 20 gm. in 30 days : 1 gm. daily for the first 10 days, and the same dose on alternate days for the succeeding 20 days. The relapses increased to 11·2 and the author concludes that this progressive rise is to be ascribed to the reduction in the total amount of quinine given. *H. H. S.*

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This Special Malaria Number contains ten articles in Chinese, three of which have been published in English : the English summaries which are given are not very informative. It appears that 20 species of Anopheles have now been reported in China. *A. G. B.*

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BLACKWATER FEVER.

Macleod (N. C.). **Report on Blackwater Fever in Uganda for 1931.**—*Uganda Protectorate Ann. Med. & San. Rep. for Year ended 31st December, 1931.* Appendix III. pp. 72–76. With 1 chart.

During the year 1931, 162 cases of blackwater fever were reported in Uganda. There were 13 Europeans, 142 Asiatics, and 7 Africans. A table is given showing the number of cases, deaths, and case mortality in Uganda during each of the last 20 years. [This table shows—as also did Ross's similar table for Rhodesia—that the death rate during the last four or five years of the period is quite as large as that during the first four or five years]. Information regarding the incidence of blackwater fever at the various stations throughout the Protectorate, and of the monthly variations in the occurrence of the disease, and the influence of age, race and sex, is summarized in a series of tables. Of the 13 cases which occurred amongst Europeans, two had been between 2 and 5 years in the country, five between 5 and 10 years, one between 10 and 15, and four between 15 and 20; in one case, no information was available. The blood was examined in 97 cases, and malaria parasites, usually *P. falciparum*, were found in 52 of them.

W. Yorke.

Giglioli (Giorgio). **Quartan Malarial Nephritis and Malarial Haemoglobinuria as Family or House Diseases in the Interior of British Guiana. Field Observations on the Epidemiology and Etiology of Blackwater Fever.**—*Riv. di Malariologia.* 1932. Vol. 11. No. 4. 29 pp. With 1 map & 2 charts. [15 refs.]

The following are the conclusions :—

" 1. Data have been collected in the field, during nine and a half years, on the epidemiology of quartan malarial nephritis and blackwater fever in the Demerara River district in the interior of British Guiana. The district has a population of approximately 6,500 comprising various races. The typical settled populations of the region is constituted by mixed races. This population is very subject to malaria and is susceptible to malarial nephritis and haemoglobinuria.

" 2. Quartan malaria is relatively a rare infection in the district, representing only 4·1 per cent. of malarial infections seen in our Hospital.

" 3. Quartan malarial nephritis affects individuals of all ages, but is much more frequent in children. Thirty cases have been studied.

" 4. Quartan malarial nephritis tends to recur with striking frequency in certain households. Five families accounted for 54 per cent. of all cases seen among the children in the district. Such a condition has been traced to house infection due to *P. malariae*.

" 5. Sixty-one cases of blackwater have been observed, the incidence of the disease is proportionate to the incidence of new malarial infections. The epidemic curve demonstrates that blackwater is not related to chronic malaria, but to new or recent infection.

" 6. Individuals of mixed race and children are most frequently attacked. Negroes and adults, in general, less frequently but when affected are more severely attacked and suffer a higher mortality.

" 7. There is a marked tendency for cases of blackwater to occur in a given locality at approximately the same period. The sequence of cases is in accordance with what might be expected if the disease were transmitted from one case to the other by means of Anopheles, also taking into consideration the conditions of relative immunity presented by a large part of the population of the endemic area, as evidenced by the lower susceptibility of adults and of the Negro race.

"8. Family and house recurrence of blackwater which has been observed in most countries where this disease has been studied, is a striking feature of haemoglobinuria in this district. Eight families accounted for over one-third of all cases seen. By analogy with what has been proven for quartan malarial nephritis, and on other general epidemiological grounds, family and house recurrence of blackwater has been ascribed to house infection.

"9. House Malaria infection occurs, when Anopheles which have become infected in that same house by feeding on an individual harbouring gametes in his blood, remain in the house for a time sufficient to ensure the maturation of sporozoits, and by feeding on other members of the family transmit the infection. *In House Malaria it is the same strain that gets transmitted.*

"10. The admission of a malarial house infection characterized by haemoglobinuria, in a district where malaria is hyperendemic, and subtertian prevalent, but haemoglobinuria is relatively rare, necessarily implies house infection which is not identifiable with ordinary malaria. In the absence of adequate parasitological knowledge, and given the general clinical and epidemiological characteristics of the disease one is led to admit that blackwater, as suggested by NOCHT, should be the direct consequence of infection with certain strains of the various Plasmodia, morphologically indistinguishable from the ordinary forms, but characterized by the biological property of producing haemolysis." *W. Y.*

CHARTERS (A. D.). **House Infection in Blackwater Fever.** [Correspondence.]—*Lancet.* 1932. Oct. 15. p. 867.

In this letter the author gives examples which he encountered in Uganda suggesting that certain houses predispose to blackwater fever. He considers that :—

"These observations strongly favour the importance of chronic subtertian malaria, which is the prevalent form encountered in this district, in the aetiology of blackwater fever, and the view that certain houses predispose to the disease by reason of the shelter which they offer to the infected anopheles mosquito." *W. Y.*

OTT. Les deux types d'évolution de la fièvre bilieuse hémoglobinurique au Laos. [**Two Types of Blackwater Fever at Laos.**]—*Ann. de Méd. et de Pharm. Colon.* 1932. July-Aug.-Sept. Vol. 30. No. 3. pp. 532–545. With 6 charts.

The ictero-haemoglobinuric syndrome observed in Laos comprises two categories of fever of quite different evolution. The first without doubt appertains to old malarial infection, and the second possibly has some other etiology.

Details are given of a patient who, at an interval of forty days, suffered from two febrile attacks which were treated by quinine and followed immediately by haemoglobinuria. Although parasites were not found, the author believes that they were definitely of malarial origin as the fever was quickly cured, on both occasions, by the judicious administration of quinine. An account is then given of a second case falling into the same category.

In contrast with these two observations in which the evolution of the blackwater has to be traced to malaria, a third case is cited in which the course was much longer and more complex, and of difficult interpretation. This case, the author states, will give an impression of the second type of bilious haemoglobinuric fever which he has encountered several times at Vientiane, but which appears exceptional in other parts of Laos. The patient, who had been at Laos for about 4 years,

had contracted malaria and had been successfully treated with quinine : he had never had blackwater fever. On Nov. 8th, 1930, after a prolonged period of good health, he was smitten with a sudden attack of fever and two days later was admitted to hospital. Between 8th and 11th Nov. he was given 2·3 gm. of quinine, and on 12th Nov. he passed blackwater and continued to do so until 15th Nov. The temperature remained slightly raised until 18th Nov., when a series of considerable oscillations commenced, and on 19th Nov. he again passed blackwater. The haemoglobinuria soon passed off, but the patient continued to run considerable temperatures and had two further slight attacks of blackwater. On 25th Nov., when the patient passed haemoglobinuria for the fourth time, a few *P. vivax* were found in the blood. After this there were no further attacks of blackwater, but the patient continued to run a temperature for many weeks notwithstanding the administration of quinine. On 9th Dec., and on several subsequent occasions, spirochaetes were found in the blood by the triple centrifugation method of examination. It was consequently decided to try the effect of an arsenical preparation and three injections of acetylarsan were given, but as each was followed by a rise of temperature the attempt was abandoned. In a second case of a like nature spirochaetes were also found.

Guineapigs were injected with the blood of these two cases. It is recorded that some of these animals died in a few days, others died after a slow infection (20–30 days) and still others survived, but blood from these when injected into a second series of guineapigs produced a fatal infection.

Those animals, which died rapidly, showed a continued loss of weight, and after a brief rise the temperature fell as rapidly as the weight. Those which resisted longer exhibited alternately loss of weight and then a return to the normal weight ; like the former animals they died in a state of cachexia with low temperature.

All the animals showed the same pathological lesions, viz., generalized visceral congestion ; no parasites to be seen ; the organs showed an intracellular and intramuscular ochre-coloured pigment which gave the Prussian blue reaction. No spirochaetes were discovered in the guineapigs ; but the author considers that the changes he has found prove the existence in his patients of a virus, other than Plasmodium, capable of producing in the guineapigs an intravascular haemolysis.

Ott believes that this case shows that there exists at Laos a type of blackwater which is not of malarial origin ; it is seasonal (autumn and winter) ; it resists quinine and arsenic and the prognosis is grave. [Obviously all this will require confirmation before it can be accepted.]

W. Y.

Feyte (R.). Deux cas de fièvre bilieuse hémoglobinurique. [**Two Cases of Blackwater.**]—*Bull. Soc. Path. Exot.* 1932. July 6. Vol. 25. No. 7. pp. 831–833.

Clinical details are given of two cases of blackwater fever; these call for no special comment. In the second case three estimations of the amount of cholesterin in the blood were made with the following results :—

1. The acute stage : cholesterin 1 gm. per litre.
2. During convalescence : cholesterin 1·16 gm. per litre.
3. After the end of the disease : cholesterin 1·8 gm. per litre.

These figures show that the titre of cholesterin increased as the patient recovered. The author states that this agrees with the findings from Indo-China [this *Bulletin*, Vol. 23, p. 553 and Vol. 29, p. 666] that good results follow the administration of a rapidly diffusible, aqueous preparation of cholesterin, viz., the chlorhydrate of choline. *W. Y.*

GUPTA (B. M. Das). **A Case of Blackwater Fever treated by Atebrin.** —*Indian Med. Gaz.* 1932. June. Vol. 67. No. 6. pp. 330–331. With 1 chart in text.

Clinical details are given of a case which, in the author's opinion, indicate that atebrin may be of value in cases of blackwater fever where the patients are intolerant of quinine. The patient, a Hindu, aged 13, was admitted to hospital on the 21st Jan., 1932, with a history that two weeks previously he had suffered from haemoglobinuria. On admission the urine was normal, but the blood contained scanty *P. falciparum*. Two doses of 5 grains of quinine were administered and were immediately followed by an attack of blackwater fever. Haemoglobinuria continued for 4 days, and the patient became convalescent. On the 16th Feb. there was a slight rise of temperature and the next day *P. falciparum* was again found in the blood. It is stated that there was marked jaundice, but no haemoglobinuria. On the 20th Feb. atebrin, 0·1 gram twice daily, was given for 5 days ; the parasites disappeared and all symptoms subsided.

In the discussion which follows this narrative, the author writes " There seems little reason to doubt that, had quinine been administered during his third attack of fever, haemoglobinuria would have resulted." [This statement is, of course, not justifiable ; the patient might have developed haemoglobinuria, but, on the other hand, he might not.] *W. Y.*

PATERSON (James C.). **The Value of Plasmochin in the Treatment of Malarial Infections encountered in Some Cases of Blackwater Fever and Quinine Haemoglobinuria.**—*Amer. Jl. Trop. Med.* 1932. Sept. Vol. 12. No. 5. pp. 363–368.

The author has examined the blood for malaria parasites in 16 consecutive cases of blackwater fever at the El Centro (? Colombia) hospital. In six of the cases malaria parasites were found, *P. falciparum* five times and *P. vivax* once. It is remarked that the parasites were present in such numbers that they could be demonstrated on the second day of the disease after a large number must necessarily have been destroyed as a result of the initial haemolysis. [What evidence is there in support of this dogmatic statement ?] The author continues by saying that the question naturally arose whether or not this complication should be treated ; and when three of the six positive cases showed subtertian rings in such profusion that life seemed to be actually threatened, there appeared to be no choice in the matter, Details are given concerning four cases in which plasmochin was given. The other two cases were treated with quinine only, but the drug was withheld until the course of the disease was well advanced ; one of these patients died, and the author considers that death may have been partly due to the fact that the severe subtertian infection which was present was ignored for three days until it was considered safe to begin quinine therapy. Two of the four cases treated by plasmochin were severe infections and could not

be safely left until the haemoglobinuria had subsided and quinine could be given without the risk of producing further haemolysis. The use of quinine in the acute stage of the disease is undoubtedly dangerous, but plasmochin while not so effective in attacking a subtertian parasite seems to have sufficient action to control most infections until quinine can be safely given.

The author summarizes his paper as follows:—

"1. Malarial parasites were encountered in 37·5 per cent. of a series of 16 consecutive cases of blackwater fever and, in all but one, the subtertian form was the offender.

"2. Three of the 6 positive cases showed subtertian ring forms in such abundance that active anti-malarial measures appeared to be imperative.

"3. Quinine cannot be safely administered to such cases of blackwater fever because of the danger of producing further haemolysis. On the other hand, plasmochin can be safely used at any stage of the disease and apparently possesses sufficient action to control the infection until such a time as quinine can be given. This drug should be equally useful in treating malaria attacks in individuals who suffer from haemoglobinuria as a result of quinine intolerance." *W. Y.*

GIGLIOLI (George). **Immunity in Blackwater Fever.**—*Riv. di Malariologia.* 1932. Vol. 11. 27 pp. With 4 figs. [15 refs.]

The following abstract is given:—

"In the present paper, which is a continuation of the other which appeared in Number 4—1932 of this same Review [*ante*], the author treats further of the epidemiology of blackwater in the interior of British Guiana.

"The incidence of the disease in the different races inhabiting the region and in the various age groups, receives particular attention. The Negro race enjoys a very marked immunity. The adult section of the settled population also presents a distinct degree of immunity.

"The clinical course of the disease in children and in adults, the occurrence of relapses, the relative mortality in the different races and age groups are also examined.

"The author concludes that definite and specific immunity to blackwater exists, and that it manifests itself with the same modalities and limitations which are known to exist as regards immunity to malaria. It is not immunity to infection, but immunity towards its clinical manifestations.

"Immunity in conclusion, and the distribution and incidence of the specific haemolytic strains of malaria parasites, are the fundamental factors which govern the epidemiology of blackwater: it is the degree of immunity of the subject in fact which determines, case by case, if infection is to be followed or not, by the culminating clinical manifestation of the disease, haemoglobinuria.

"It appears probable that 'mute' or clinically negative, and therefore unrecognisable infections with haemolytic strains, particularly in certain tropical regions, should not be rare; such infections represent the source, the reservoir, of those same infections, which in non-immune subjects, in Europeans for instance, make themselves dramatically evident with the dreaded syndrome of blackwater fever." *W. Y.*

OTT. Recherches sur la pathogénie et le traitement de la fièvre bilieuse hémoglobinurique. Considérations sur la pathogénie du syndrome. [**Pathogeny and Treatment of Blackwater Fever.**]—*Bull. Soc. Path. Exot.* 1932. July 6. Vol. 25. No. 7. pp. 735–747. With 1 fig.

The author devotes himself to an analysis of the factors which may be responsible for the haemolytic process in blackwater

fever. While a good deal of it is theoretical, the author marshals a considerable number of experimental observations, made by himself and others, in support of his contentions. The first portion of the article deals with the rôle of hypocholesteraemia and the second part with the rôle of precipitating factors. The main argument can be summarized as follows :—

Cholesterin inhibits, in the animal organism, the lytic action of disintegration products of the lipoids (fatty acids, lysocithins). The cholesterin titre is lowered in malaria and particularly so in blackwater fever. The erythrocytes of blackwater fever patients exhibit a peculiar sensitiveness to various haemolytic agents ; quinine, which, in therapeutic doses, is unable to provoke haemolysis, acts much more efficaciously in the presence of any other haemolysin (sensibilisatrice, lysocithin, etc.).

The author inquired whether from these facts it is not possible to elaborate a satisfactory theory of the pathogenesis of blackwater fever.

The physico-chemical equilibrium of the different components of the blood is destroyed, in chronic malaria, by the improverishment of the erythrocytes in cholesterin. The red cells, deficient in cholesterin, yield up their haemoglobin owing to the action of fatty acids and lysocithins normally occurring in the circulation. This state of affairs arises in certain forms of chronic malaria where, following a red cell fragility, the ictero-haemolytic syndrome gradually develops: but in these cases the degree of haemolysis does not habitually succeed in raising the haemoglobinaemia up to the level of the renal threshold. However, in such patients a simple access of fever, owing to the modifications in the physico-chemical state of the serum which it produces, will suffice to cause haemolysis of such a number of red cells that haemoglobinuria results.

When hypocholesteraemia does not suffice to produce haemoglobinuria, the sudden addition of a supplementary haemolytic agent will raise the lytic titre to the level necessary to destroy the red cells which had hitherto resisted the organic lysocithins ; quinine, even in small doses, will act in this way as has been shown by Nocht and Kikuth, and others.

Marcel Leger, in the discussion which followed this paper, stated that for many years he had made a point of determining the degree of cholesteraemia in numerous patients. He referred to three cases of sleeping sickness in whom, before any treatment was given, the cholesteraemia was below 1 gm. per litre—in one of them it was only 0·58 gm. All three had suffered from febrile disturbances and, before the true diagnosis was made, had been given large doses of quinine ; one had in fact received 52 consecutive intramuscular injections. None of these patients exhibited any signs of haemoglobinuria. *W. Y.*

Brahmachari (Phanindranath), Banerjea (Radhakrishna) & Brahmachari (Upendranath). **Studies in Blackwater Fever.**—*Jl. Trop. Med. & Hyg.* 1932. Oct. 15. Vol. 35. No. 20. pp. 309–310.

Experiments were conducted to determine the action of quinine bihydrochloride and quinine hydrochloride, in various strengths, *in vitro* upon the haemolytic system. The results, which are given in tables, show that the solutions of the quinine salts, in strengths not

having any direct haemolytic action, inhibit haemolysis in the haemolytic system. From these facts the authors argue that if a haemolytic system plays a part in the haemolysis of blackwater fever, then it is possible that the administration of quinine might inhibit the haemolysis.

W. Y.

McCulloch (W. C.). **The Biochemical Aspect of Blackwater Fever.**—*West African Med. Jl.* 1932. July. Vol. 6. No. 1. pp. 8–11. [14 refs.]

This paper, which is entirely of a theoretical nature, cannot easily be summarized and must be consulted in the original by those interested.

W. Y.

SLEEPING SICKNESS.

LEE (S. W. T.). **Report on Sleeping Sickness for the Year 1931.**—*Uganda Protectorate Ann. Med. & San. Rep. for Year ended 31st December, 1931.* Appendix IV. pp. 77–81.

The incidence of sleeping sickness for the last six years in Uganda is shown in a table, and in a second table the number of deaths attributed to the disease, during the last 27 years, is given. Information is recorded regarding the staff available for sleeping sickness work in Uganda and also regarding slight changes in the 1928 sleeping sickness ordinances. The distribution of cases of sleeping sickness in the various districts during 1931 is briefly discussed and the main facts summarized in tabular form. It appears that the number of new cases of sleeping sickness has steadily declined since 1929. Mr. C. W. CHORLEY is continuing his experiments on the trapping of *G. palpalis*. From the results obtained so far, it appears probable that some of the traps designed by Mr. Chorley will be of great practical value. It is proposed to endeavour to clear one island of *G. palpalis* by using a number of traps, and, if this proves successful, an attempt will be made to clear a suitable area of the foreshore of the lake. *W. Yorke.*

DE MARQUEISSAC. Fonctionnement des équipes de prospection et de traitement du secteur de prophylaxie de la trypanosomiase au Togo. [**Survey and Treatment Brigades in the Prophylaxis Sector of Trypanosomiasis in Togo.**]—*Ann. de Méd. et de Pharm. Colon.* 1932. July-Aug.–Sept. Vol. 30. No. 3. pp. 478–487.

An account is given of the machinery which has been evolved for dealing with sleeping sickness in the Bina river district of Togo. The article should be consulted in the original by those interested.

W. Y.

DUKE (H. Lyndhurst). **The Polymorphic Trypanosomes of Damba Island, Victoria Nyanza. I.–Their Ability to infect Man.**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 191–206.

The author points out that before the great epidemic of sleeping sickness swept through Busoga and Buganda in the early years of the present century, the island of Damba was thickly populated. Conditions were ideal for the rapid spread of human trypanosomiasis and the people suffered heavily before the survivors were removed to the mainland towards the end of 1909. While the island was inhabited the situtunga were strictly confined to the papyrus and grass swamps. After the evacuation of the island the situtunga began to multiply rapidly. As the antelope multiplied it came more and more into contact with tsetse and the fly followed them into the forest and penetrated the island from end to end. Experiments in 1910 and 1911 showed that *T. gambiense* can survive in antelope for at least 22 months in a form transmissible by tsetse, so that it is justifiable to conclude that once introduced into the situtunga this trypanosome would have an excellent chance of survival. It is not known whether *T. brucei* occurred on the northern islands of Lake Victoria ; if it did, the cattle must have been its principal host, because the antelope was, in the early days, protected from the fly by its habits and habitat. The cattle were, of course, all removed at the same time as their native owners.

In 1912, Duke expressed the opinion that three strains isolated from situtunga or *Glossina palpalis* on Damba were descendants of the human

trypanosome which decimated the population of Damba. It was expected that the sojourn in the antelope would sooner or later exert an effect on the attributes of the trypanosome. Duke believes that signs of such modifications were discernible in 1920. Three 1932 strains are now being carefully examined, and it is already evident that in one important aspect at least they differ from the earlier strains, the change being still in the direction of a closer resemblance to *brucei*. The ability of these three recently isolated strains to infect man is therefore a point of considerable interest.

The three strains that form the subject of this paper were recovered by feeding on clean monkeys wild *G. palpalis* caught on the shore of Damba Island. The three strains are designated Strain 910, Strain 911, and Strain 912 respectively. Of the three the last proved the most readily transmissible by *G. palpalis*. Laboratory bred *G. palpalis*, cyclically infected with one or other of these three strains, were fed upon four normal human beings, three natives and one European. One native was exposed to infection by all three strains, the other volunteers to two strains each ; none of them became infected.

In the discussion which follows the record of these experiments Duke writes :—

" The realisation that the Damba trypanosome, and, in all probability, the similar strains carried by *G. palpalis* along the whole northern littoral of Lake Victoria, are innocuous to normal man simplifies considerably the task of reclaiming this fertile territory.

" Attention can now be concentrated wholly on keeping out the human reservoir of the disease in the shape of infected natives from neighbouring foci of human trypanosomiasis."

Duke then passes to a consideration of arguments in support of his theory that *T. gambiense* on Damba Island, on the disappearance of man, adopted the situtunga as its principal mammalian host, and has survived in the antelope, with certain modifications, until the present day. He believes that on this assumption the greatest changes in the trypanosome are to be associated with the actual transition period, whilst the parasite was still engaged in adapting itself to the new host. This he considers to be an answer to a former criticism by the reviewer to the effect that the differences in pathogenicity between his 1912 and 1920 antelope strains were distinctly less than those between the 1912 antelope strains and the strain of *T. gambiense* derived from man. Duke further states that there is as yet no unequivocal evidence that a trypanosome recovered from man's blood may lose its power of infecting man. Whether or not this happens in nature is the main problem of trypanosomiasis research to-day. He does not believe that the *in vitro* technique of the reviewer and his colleagues can be regarded as infallible for settling this point, and he quotes recent observations of Corson and of Adams in support of this contention.

[This paper must be consulted in the original by those interested.]

W. Y.

Taylor (A. W.). **The Development of West African Strains of *Trypanosoma gambiense* in *Glossina tachinoides* under Normal Laboratory Conditions, and at Raised Temperatures.**—*Parasitology*. 1932. Oct. Vol. 24. No. 3. pp. 401–418. With 4 figs. on 1 plate. [23 refs.]

In his introduction the author refers to the well known difficulty of infecting species of Glossina with *T. gambiense* under laboratory

conditions. Work described in this paper was planned in order to study the infectivity to *G. tachinoides* of a representative selection of strains of *T. gambiense* from West Africa with the particular object of determining whether non-transmissible strains occur there as frequently as, according to DUKE, they do in East Africa. In addition it was decided to examine possible factors influencing the *T. gambiense* infection rate in Glossina.

The following is the author's summary :—

" 1. An account is given of the development of strains of *Trypanosoma gambiense* in *Glossina tachinoides*.

" Complete development with infection of salivary glands and hypopharynx occupies from 12 to 40 days and upwards, according to the strain of trypanosome used and the temperature conditions during development.

" 2. It is shown that the first or intestinal phase of development is passed within the extra-peritrophic space and that the lumen or intra-peritrophic space of the gut is not involved.

" 3. The importance of the proventricular infection as an index of maturing infections is stressed, and it is shown that filamentar crithidia are always present in this organ in the later stages of infection when infection of salivary glands is taking place. It has been proved that these filamentar crithidia may constitute up to 20 per cent. of flagellates in the proventriculus and are partly responsible for the further migration to the salivary glands.

" 4. An account is given of the infectivity to *G. tachinoides* of twenty-six strains of *T. gambiense* from epidemic and endemic sleeping sickness areas in Northern Nigeria. None of the twenty-six was proved to be non-transmissible and twenty-five of the strains gave Total Infectivity Rates in the tsetse of from 0·9–10·5, the Cyclical Developmental Rates ranging from 0·6–9·8.

" 5. No evidence has been obtained that strains of *T. gambiense* from chronic cases of human trypanosomiasis in endemic areas are less transmissible by tsetse than strains originating in epidemic areas.

" 6. An account is given of experiments in which *G. tachinoides* infected with *T. gambiense* were exposed to 37°C. for varying lengths of time. The effect of high temperature during the infecting period is seen in a marked and constant increase in the proportion of tsetse infected. In the case of one strain a total infection rate of 77·8 per cent. was obtained with true cyclical development in 73·5 per cent. of the tsetse used.

" 7. It is suggested that the temperatures at which experimental tsetse are infected in the laboratory with *T. gambiense* are excessively low, and an investigation is to be made into the optimum climatic conditions for development of the trypanosome in the fly with a parallel attempt to correlate this with the climatic conditions under which wild tsetse become infected in nature."

[This interesting and important paper should be consulted in the original by all working on the subject.] *W. Y.*

MONTESTRUC (E.). Infection et réinfection trypaniques chez un Européen (auto-observation). [**The Author's Infection and Reinfection with Trypanosomes.**]—*Bull. Soc. Path. Exot.* 1932. June 8. Vol. 25. No. 6. pp. 664–668.

Clinical details are given concerning the patient (a Colonial Medical Officer) who contracted sleeping sickness in Cameroons at the beginning of 1927, and, after having been cured, became reinfected recently whilst on a tour on the Niger river. JAMOT, who commented on the case, states that it presents several points of interest. The first question of importance was whether the symptoms, which developed

in January, 1932, were due to a relapse or were the result of a reinfection ; analysis of the evidence indicates that they were probably due to reinfection. In the second place it is interesting to contrast the condition of the patient when the first attack was diagnosed, with his condition at the time the second attack was recognized. On the first occasion he complained of no symptoms and diagnosis was made accidentally in the course of routine examination ; on the second occasion the disease started suddenly with a rigor, fever, severe vomiting, and pronounced asthenia. These two groups of symptoms—the one benign and the other severe—correspond with the two great clinical types which are met with at the beginning of the disease. Another point worthy of note is the fact that the patient exhibited a large purpuric area on the dorsum of the left foot, and at the same time enlarged and painful popliteal and crural glands. Unfortunately, these glands were not punctured, but under the influence of treatment they disappeared coincidentally with the purpuric condition. This fact seems to suggest that these abnormal morbid manifestations resulted from the infection. The usual primary manifestation is, however, a non-suppurative furuncle. The furuncle is an expression of the defence of the organism at the point of inoculation ; the glandular enlargement usually develops slowly and is painless. Jamot considers that possibly a patient who had already suffered from one attack of the disease and who was weakened by fatigue and long service in the tropics might react less energetically than normally. *W. Y.*

Guyomar'ch. Méningite trypanosomiasique avec amaurose guérie par la tryparsamide. [**Trypanosomal Meningitis with Amaurosis cured by Tryparsamide.**]—*Marseille-Méd.* 1932. June 25. Vol. 69. No. 18. pp. 822–826.

Details are given of a patient who contracted sleeping sickness in his native country—the Ivory Coast. He was recruited in February, 1930, and sent first to Senegal and then to Algiers ; the first manifestations of the disease—headaches, stiffness, and pains in the limbs—did not manifest themselves until six months later and their true nature was not recognized. The patient was considered to be a syphilitic because the blood Wassermann reaction was strongly positive, and antisyphilitic treatment was administered. This treatment had, however, no effect and the condition progressed ; the patient developed meningeal symptoms with grave bilateral optic atrophy. In January, 1932, he was sent to hospital at Marseilles preparatory to repatriation. Here a lumbar puncture revealed the presence of trypanosomes in the spinal fluid. Notwithstanding the optic atrophy a course of tryparsamide was given ; the initial dose was 1 gm. and at the third injection the dose was increased to 3 gm. When he had received a course of 36 gm. the condition had completely changed, and the acuity of vision had steadily improved. *W. Y.*

van den Branden (F.). Influence défavorable d'un traitement insuffisant et irrégulier sur les résultats obtenus avec le tryponarsyl dans le traitement de la trypanosomiase humaine chronique. [**Unfavourable Influence of Insufficient Treatment with Tryponarsyl on Subsequent Treatment.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. Oct. 30. Vol. 12. No. 3. pp. 375–378.

Whilst revising his record of old chronic cases of sleeping sickness, treated at Leopoldville, van den Branden encountered a number of

protocols which seemed to show that insufficient and irregular preliminary treatments exerted an unfavourable influence on subsequent efficient courses of tryparsamide.

Details of 5 such cases are given ; all received various treatments with atoxyl and tartar emetic and, some time later, long courses of tryparsamide which failed to cure. The author admits that it might be argued that he would have failed to cure these cases even if they had not been previously unsuccessfully treated ; but comparison with the results obtained in previously untreated cases (about 60 per cent. cures) makes this doubtful. He believes that arsenic-resistance produced by the initial treatments plays a part in the subsequent failure to cure with tryparsamide. *W. Y.*

MACLEAN (George) & FAIRBAIRN (H.). **Treatment of Rhodesian Sleeping Sickness with Bayer 205 and Tryparsamide : Observations on 719 Cases.**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 157–189. [17 refs.]

In the first part of this paper, the authors summarize briefly the results obtained by various workers in the treatment of *rhodesiense* sleeping sickness with Bayer 205 and tryparsamide respectively. The series of cases described in the present paper were mostly from the Tabora Province of Tanganyika Territory during the first and second years of an epidemic which swept the northern part of this Province between 1927 and 1930. The other cases occurred between 1925 and 1927 in Mwanza. There were 873 cases in the original series, but for various reasons records of 91 had to be discarded. Furthermore, 63 cases could not be traced in 1931. The survivors of the remaining 719 cases have all had their general clinical condition and also their blood and cerebrospinal fluid examined from time to time since completing treatment. They have been kept under observation for a minimum period of two years and five months from the time they commenced treatment, and some of the Mwanza cases had been observed for more than $6\frac{1}{2}$ years.

The following summary is given :—

" The treatment of seven hundred and nineteen cases is analysed, and it is shown that with adequate administration of Bayer 205 (4–5 grammes in 1 gramme weekly doses) as many as 73·5 per cent. may recover and remain well for a period of twenty-nine or more months, provided treatment is begun within a month of the onset of symptoms. This drug is effective in the early stages of infection of the cerebro-spinal fluid. Generally speaking the earlier the case the better the chance of cure, and if an uncomplicated case is treated at the onset of symptoms complete recovery is practically certain.

" It is also shown that a number of cases recover after administration of tryparsamide alone, but it is much less rapid, less effective and less constant in its results than the former drug.

" There is no conclusive proof, from a study of these cases, that combined treatment with Bayer 205 and tryparsamide gives better results in moderately advanced cases than the former drug alone, but what evidence there is, supports the view that the combination is an advantage in late cases.

" At a time when cases came for treatment at a more advanced stage of the disease than they generally do now, it was found that none of the cachetic cases ever recovered after the administration of Bayer 205 alone, whereas a few did so after the combined treatment.

" For these reasons, combined treatment should always be given when the prognosis is in doubt, particularly as the records suggest that there are some strains or phases which respond specially well to tryparsamide.

" The dose of tryparsamide should be 2–4 grammes in adults and a total dosage should be at least 22 grammes.

" Except in relapses, where the results are not comparable with those obtained in previously untreated cases, we have a very limited experience of more intensive or prolonged administration of Bayer 205 than that described above.

" It is possible that more intensive treatment would give better results in cases in whom the prognosis is doubtful.

" Neither age, sex nor a common intercurrent disease like ankylostomiasis has been found to have any material influence on the results of treatment.

" The toxic effects of Bayer 205, when administered as described, are rarely of practical importance.

" The toxic effects of tryparsamide are more serious and cannot always be guarded against. In relapsed cases, who appear to be more susceptible, the initial dose should not exceed 2 grammes.

" Prognosis is best arrived at by observing the condition of the patient just before treatment, the chief points to be noted being the duration of the illness, the state of the general health and the condition of the cerebro-spinal fluid. Examination of the patient a few weeks or months after termination of treatment may give quite deceptive results."

[This paper, which contains much important information, must be consulted in the original by those interested.] *W. Y.*

DE MARQUEISSAC. Propriétés du 205 Bayer-309 Fourneau (moranyl) dans la thérapeutique curative de la trypanosomiase humaine. [**Moranyl in the Therapy of Human Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1932. Oct. 12. Vol. 25. No. 8. pp. 898–902.

The author believes that in the majority of cases moranyl can transform a race of trypanosomes, which have become insensitive, into a sensitive race, and that in all cases it can attenuate the virus on which arsenical remedies have proved to be impotent. In support of this contention he quotes two cases recorded by Miss PEARCE in her monograph and three cases of his own. [On the face of it Miss PEARCE's cases are not quite parallel with de Marqueissac's. Miss PEARCE's cases apparently resisted a first course of tryparsamide and later, after a course of Bayer 205, which was said to be without effect, were cured by a second course of larger doses of tryparsamide. Miss PEARCE herself attributes the success of the second course to the fact that larger doses were used, but de Marqueissac writes that in reality the course of Bayer exercised an unfavourable action on the parasites, so rendering them an easy prey to the second course of tryparsamide.] De Marqueissac's three cases differ in that they were all cured by Bayer after several unsuccessful attempts with arsenicals.

The second part of this paper is concerned with a brief discussion of the valuable results obtained by the simultaneous administration of Bayer and tryparsamide. Veritable resurrections were obtained with the combined treatment consisting of moranyl 0·5 gm. + tryparsamide 0·5 gm. The moranyl is first injected, and then, without withdrawing the needle, the tryparsamide. The treatment is given every four days and no ill effects were seen. *W. Y.*

DE MARQUEISSAC. Emploi du 270 Fourneau (orsanine) en prophylaxie itinérante dans le secteur de Pagouda (Togo). [**Itinerant Prophylaxis in Togo with Orsanine.**]—*Bull. Soc. Path. Exot.* 1932. Oct. 12. Vol. 25. No. 8. pp. 902–905.

In view of the encouraging preliminary results obtained with orsanine, it was decided to use this drug in the treatment of all new cases found in the Pagouda sector of Togo. In all, between 1st March and the 1st June, 1932, the drug was given to 890 subjects ; 10 subcutaneous injections were given and the immediate result was a peripheral sterilization in 100 per cent. Notwithstanding the fact that during the three months 9,153 injections were given, the number of accidents, ocular and local, was infinitesimal. The relatively few deaths (4 out of 890 patients) may perhaps be attributed to a progressive arsenical intoxication, and indicate that a certain total dosage (200 mgm. per kilo. for the adult, and 150 mgm. per kilo for old people) should not be exceeded.

W. Y.

PARIS EGUILAZ (Higinio). Contribucion al estudio de los resultados tardios en el tratamiento de la tripanosomiasis humana. [**The Late Results of Treatment of Human Trypanosomiasis.**]—*Medicina Países Cálidos.* Madrid. 1932. Sept. Vol. 5. No. 5. pp. 371–407. [83 refs.]

Much of this article is of the nature of a clinical lecture on trypanosomiasis ; the author describes some of the many clinical syndromes which may be met with—glandular, meningitic, hypokinetic, hypertonic, myoclonic and mixed—and the results of examination of the spinal fluid. Details are next given of the various forms of treatment adopted ; atoxyl intramuscularly with tartar emetic intravenously ; tryparsamide and tartar emetic ; Bayer 205 ; and the results on small groups of patients presenting the different syndromes. The patients were from Fernando Po and the sanitary District of Tuplapla. The following are the main conclusions :—

1. Prompt treatment of patients in the period of blood and gland infection results generally in cure.

2. Comparing the results obtained with atoxyl 12 gm., tryparsamide 18 gm., Bayer 205 7·5 gm., patients in the earlier stage respond best to Bayer 205 (or Fourneau 309).

3. Only a proportion of those with the meningitic syndrome is curable (data are insufficient for a decision as to what proportion). The best drug for these patients was tryparsamide, and in arsenic-resistant cases Bayer 205. Atoxyl is useless.

4. Patients with symptoms of meningo-encephalitis usually die. With Bayer 205 transient improvement may be obtained ; atoxyl is of no value, tryparsamide should be the drug of choice since clinical amelioration lasting for a year or even longer has been observed. If in addition there are signs of dementia, tryparsamide is the only drug which the author found at all serviceable ; atoxyl was useless, and Bayer 205 often increased excitability and made matters worse.

5. In European patients a mixed treatment seemed best, Bayer 205 followed 2–3 months later by tryparsamide or vice versa.

6. Bayer 205 is very useful as a prophylactic.

This statement is based on observations of a group of 58 persons to whom the author had given 2 doses (each 1 gm.), and during the succeeding 5 months none developed the disease, whereas on contiguous estates from 7 to 10 per cent were infected. He mentions another group of 44 to whom he gave 2 doses of 1 gm. in successive weeks, with inconclusive results as observation was interrupted by their removal to other estates. *H. H. S.*

YORKE (Warrington) & HAWKING (Frank). **Studies in Chemotherapy. VII. Is the Resistance of a Drug-Fast Trypanosome modified by Transference to a Different Species of Vertebrate Host?**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 215–237. [15 refs.]

In the year 1908 MESNIL and BRIMONT studying the atoxyl resistance of trypanosomes stated that a strain of trypanosomes made atoxyl-resistant in one species of animal (mouse) lost that resistance when transferred to another host (rat). This finding, which was apparently confirmed by Liverpool workers, has profoundly influenced the minds of all who have been since engaged in studying chemotherapeutic processes, as the authors show by a number of quotations. They noted, however, that no one has of recent years studied the matter experimentally, and since it is of obvious importance when one seeks to ascertain whether the trypanosomes in treated patients are drug-fast or not (on the French authors' theory it would be useless to test that property in inoculated animals) the English authors devote this paper to an experimental re-examination of the question. They used the atoxyl-resistant strain of *T. rhodesiense* referred to in their previous papers and give a number of tables which should be studied by all who are interested. After giving the results of their investigation, in which they entirely failed to confirm the French authors, they subject MESNIL and BRIMONT's work to a detailed criticism. The gist of this is that they failed to keep before them the fact that resistance is relative; that they employed strains with a comparatively slight degree of resistance; that they used atoxyl which is (for reasons stated in the paper) ill-adapted for the purpose; that they failed to interpret correctly the fact that the same dose of atoxyl has by no means invariably the same effect on different mice infected with the same strain. The authors' summary is as follows:—

"1. Reference is made to the observations of Mesnil and Brimont, and of Breinl and Nierenstein and others, to the effect that a strain of trypanosomes made resistant to atoxyl in the mouse may lose this resistance when transferred to other hosts.

"2. Study of recent reviews and articles relating to chemotherapy indicates that these observations have not only been accepted without question, but have had an important influence on modern conceptions of chemotherapeutic processes and of drug-resistance. Moreover, apart from its academic interest, the matter is one of immediate practical importance in so far as it touches the investigation of the problem whether the development of drug-resistance is a cause of the failures so frequently encountered in the treatment of human trypanosomiasis. For obvious reasons, it is practically impossible to investigate the problem by direct observations on man himself; and, if resistance is lost on the transference of the trypanosome from man to laboratory animals, the fact constitutes

a most serious obstacle to the elucidation of this fundamental question. These observations impressed upon us the necessity for re-investigating the whole subject.

" 3. Our experiments failed to confirm the observations of Mesnil and Brimont, and of Breinl and Nierenstein and others. A strain of *T. rhodesiense*, made resistant to atoxyl in the mouse, continued to manifest its full resistance when transferred to, and passaged through, rats ; as also did a strain made resistant to tryparsamide in mice when transferred to, and passaged through, rabbits ; similarly a strain made resistant to tryparsamide in the rabbit manifested complete resistance when subsequently transferred to mice. Moreover, *in vitro* experiments likewise yielded results which indicate that the character of drug-resistance is not modified by transference of the trypanosome from one host to another.

" 4. Attention is drawn to the fact that resistance is a relative term and that all degrees of resistance, varying from the sensitiveness of the normal strain to a condition of complete insensitiveness to the largest doses which can be tolerated by the host, can easily be produced. Whilst atoxyl and other pentavalent arsenicals are excellent drugs for the production of such strains they are, for reasons stated, relatively poor indicators of the degree of resistance attained by any strain. The trivalent arsenicals, halarsol and reduced tryparsamide thioglycollate, are immeasurably superior in this respect, and enable the degree of resistance to aromatic arsenicals, attained by a strain of trypansomes, to be assessed with great accuracy and within wide limits.

" 5. We have subjected the papers of Mesnil and Brimont, and of Breinl and Nierenstein to critical examination, and, for reasons stated, have reached the opinion that the data supplied therein warranted neither the sweeping generalization of Breinl and Nierenstein ' dass die erworbene Atoxylfestigkeit nur für die betreffende Tierspezies gut hält, in welcher die Atoxylfestigkeit erworben wurde,' nor even the more modest conclusion of Mesnil and Brimont : " Nos expériences comparées chez le rat et la souris prouvent en plus que le milieu-hôte a une grande importance ; pour être exact, il faut dire que la race est résistante *dans un organisme donné*."

" 6. Our investigations convince us that resistance to the aromatic arsenicals is a stable character which is inherent in the trypanosomes themselves, and is in no way dependent upon, or modified by, the particular vertebrate host in which the parasite happens to find itself. The trypanosome is resistant to the drug itself, or, in the case of a pentavalent arsenical, to its corresponding trivalent derivative. We have found no evidence to support Breinl and Nierenstein's hypothesis that the resistance is directed against a combination of the drug and of the specific serum of the host in which the strain became resistant." *A. G. B.*

YORKE (Warrington). **Drug Resistance with Special Reference to Trypanosomiasis.**—*Brit. Med. Jl.* 1932. Oct. 8. pp. 668–670.

For the last five years the author and colleagues have been engaged in the study of chemotherapy; their results have been published from time to time and have been noticed in this *Bulletin*, the last in the present number (above). Yorke refers here to " the enormous superstructure of hypothesis which has been erected on a most insecure foundation of questionable facts " ; to such a charge the present work will not be held liable and though the ground has already been covered a fairly full account of this, a paper read at the Centenary Meeting of the British Medical Association, seems justified. The story begins with the discovery of chemo-resistance by FRANKE and ROEHL in EHRLICH'S laboratory in 1907, and the Liverpool workers have devoted themselves almost entirely to this aspect of their subject.

1. Feeling that the problem could not be satisfactorily studied *in vivo* owing to the number of variables their first aim was to find a method whereby a suspension of trypanosomes could be kept alive *in vitro*, in undiminished numbers and with unlowered vitality for at least 24 hours at 37°C.

2. By the use of the technique they worked out they compared the trypanocidal activity of organic pentavalent compounds of arsenic and antimony on the one hand and organic trivalent compounds on the other. Whereas the pentavalent compounds were but slightly trypanocidal, a solution of 1 in 1,600 being required to destroy the parasites in 24 hours, the organic trivalent compounds of arsenic were extraordinarily effective, even in a dilution of several hundred millions; sodium arsenite and tartar emetic were intermediate. This work, in conjunction with a series of experiments on infected mice, enabled them to reach the conclusion that the therapeutic action of the trivalent compounds of arsenic and antimony is dependent entirely on their amazing trypanocidal power. It is unnecessary in this case to assume co-operation on the part of the host, but the pentavalent compounds must undergo a reduction before they become effective.

3. They next tested strains of *T. rhodesiense* made resistant to atoxyl and acriflavine respectively *in vitro* and *in vivo* against a whole series of drugs—aromatic compounds of arsenic and of antimony, non-aromatic compounds of the two elements, non-metallic compounds, as acriflavine and Bayer 205. It was found that the two strains, acriflavin-resistant and atoxyl-resistant, behaved in exactly the same way, resisting all aromatic compounds of arsenic and antimony, as well as acriflavine but being sensitive to sodium arsenite, tartar emetic, and Bayer 205. Strains made resistant to other aromatic arsenicals behaved in an identical way. The general conclusion was therefore reached that if a strain of trypanosomes becomes resistant to any of the aromatic compounds of arsenic or antimony it becomes resistant to the others but not to the non-aromatic compounds. Hence the terms arsenic resistance, antimony resistance, are incorrect; the resistance is really to the various substituted phenyl radicles of the aromatic compounds.

4. They discovered that drug resistance is a stable character of the trypanosomes themselves and in no way dependent on the host (see above).

5. They studied the nature of the change undergone by a drug-fast strain of trypanosomes. They found that such trypanosomes owe their resistance to the fact that they do not *in vitro* absorb aromatic arsenicals even though these are present in concentrations rapidly fatal to normal strains.

6. Their *in vitro* experiments indicate that the development of drug resistance is fundamentally the result of a process of mutation, though selection may on occasion play a part.

7. They studied the factors conducive to the production of drug resistance. They found that it varied with different drugs—easily produced by certain aromatic arsenicals and antimonials, much less easily by Bayer 205 and not at all by tartar emetic—and also with the manner in which they were administered. The optimum conditions for the production of drug resistance are attained when the trypanosomes are repeatedly exposed to the highest concentration of drug which just fails to destroy them all.

8. Finally is discussed the question of drug fastness in man. Whether the trypanosomes in man become fast to drugs or not is unknown though it is often assumed that they do. The question is probably easy to solve by transferring the parasites to mice and testing their resistance to aromatic arsenicals in these animals. Should such resistance develop it is of great practical importance, for the character may be retained unimpaired for years, and administration of aromatic compounds of arsenic and antimony only increases the resistance. If human beings do develop drug-resistant infections we do not know certainly whether the character survives passage through Glossina, which again is of the greatest importance. *A. G. B.*

i. Nicolle (Pierre). Etude systématique de l'action synergique du 205 Bayer-309 Fourneau et de l'émétique d'aniline, sur l'infection expérimentale de la souris par *Trypanosoma congolense.* [**Synergic Action of Bayer 205 and Aniline Antimony Tartrate on *T. congolense* Infection in Mice.**]—*C. R. Soc. Biol.* 1932. Nov. 4. Vol. 111. No. 33. pp. 434–436. With 1 fig.

ii. Launoy (L.). Etat des recherches sur les synergies chimiques trypanocides. Nouveaux faits relatifs à l'étude de leur mécanisme.—*Ibid.* pp. 437–439.

i. Reference is made to the previous work of Launoy and his colleagues on the synergic action of Fourneau 309 and certain compounds of antimony [this *Bulletin*, Vol. 29, p. 644]. In the present paper Nicolle presents data suggesting that a similar synergism is seen with Fourneau 309 and aniline antimony tartrate.

ii. In the first part of this paper the author refers briefly to his previous work on the synergic action of certain trypanocidal substances He then passes to a consideration of the mechanism of synergic action. These new observations relate to certain observations—morphological and biological—concerning the action of Bayer 205 (Fourneau 309) on *T. congolense.* When a mouse heavily infected with *T. congolense* is treated with 0·005 gm. of Bayer 205 per 20 gm., the disappearance of the trypanosomes is accompanied by an intense phagocytosis. The infective power of the blood of treated mice exhibits great variations. The blood of some mice is no longer virulent after two hours, whilst that of others of the same series may be infective up to the 5th or 9th or rarely even up to the 17th hour.

As a rule, the evolution of the relapse virus is but slightly modified in the treated mouse and in the passage mouse. In certain cases, however, the relapse virus is much less virulent and the disease may run a course lasting more than six months, the host acting as a carrier. When passed into other mice, the virus is at first but slightly virulent and the virulence gradually increases in subsequent passages. The morphological changes which appear to lead to avirulence but not to sterilization are : achromatosis of the nucleus and granular degeneration of the cytoplasm.

When the relapse virus is subjected to the action of an antimonial compound it is found not to be sensitive to antimony. This fact is opposed to the antimutative theory of Morgenroth.

Launoy believes that synergic trypanocidal action is due to the prevention of the formation (if they do not already exist), of the resistant forms leading to relapses or (if they already exist) to their inhibition or destruction. *W. Y.*

i. Pieraerts (G.) & Konné (M.). Recherches sur les associations médicamenteuses à base de Bayer 205 dans les trypanosomiases. I.—Sur les modalités d'obtention de l'action thérapeutique combinée à base de B. 205. [**Association of other Drugs with Bayer 205 in Trypanosomiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. Oct. 30. Vol. 12. No. 3. pp. 281–310.

ii. ——. Recherches sur les associations médicamenteuses à base de B. 205-F. 309. II.—Sur le mécanisme de l'action thérapeutique combinée à base de B. 205.—*Ibid.* pp. 313–335. [25 refs.]

i. The authors refer to previous work indicating the advantages resulting from the association of various drugs with Bayer 205 in the treatment of experimental and human trypanosomiasis. They also recall the observation of Morgenroth [this *Bulletin*, Vol. 21, p. 757] to the effect that it is possible to obtain cures, with non-therapeutic doses of tartar emetic, in animals which, at the time of infection, had been given very small doses of Bayer 205; Morgenroth in his attempt to explain this phenomenon had postulated an "antimutative action" of Bayer 205. The present authors decided to re-investigate this phenomenon, and their work is the subject of the two papers. In the first they have attempted by varying the technique of administration of the doses and even of the drugs to ascertain the optimum conditions for the phenomenon; and in the second they have endeavoured by various means to explain its mechanism. Rats, infected with the virus Pecaudi-Tumba, which has been maintained in the Brussels School of Tropical Medicine since 1924, were used in the experiments. The results of the very numerous experiments are set forth in a long series of tables. The general conclusions reached in the first paper are as follows:—

1. It is possible with the virus Pecaudi-Tumba to reproduce the phenomenon of Morgenroth and Freund if minimum doses of 5 mgm. of Bayer and 15 mgm. of tartar emetic are used.

2. The same doses give equal, if not superior, results if the Bayer 205 be administered at the time of blood infection instead of at that of inoculation, and if the tartar emetic be given at the time of relapse.

3. Instead of awaiting the relapse the tartar emetic can be given 24 or 48 hours after the Bayer 205, but this method does not appear to be followed by a better result than is the former.

4. Tryponarsyl—a pentavalent arsenical—when given 48 hours after 5 mgm. of Bayer 205, appears to be more active than when given alone; but its action is not much increased.

5. Myosalvarsan—a trivalent arsenical—when given 48 hours after Bayer 205 is definitely more active than when given alone.

ii. The work described in the second paper followed two main lines: In the first the trypanosomes, which had been subjected to the action of Bayer 205 in a rat, were passaged into a second rat which was treated with tartar emetic; in the second these steps in combined therapy were performed *in vitro*. In his *in vitro* experiments the author followed closely the technique described by the reviewer and his colleagues [this *Bulletin*, Vol. 27, p. 237]. The results of this work are summarized as follows:—

1. Trypanosomes which had been subjected *in vivo* to the action of 5 mgm. of Bayer 205 for 12 hours, 24 hours, and 11 days, respectively, are not found, when subsequently passed to a new animal, to be more sensitive to 15 mgm. of tartar emetic than are normal trypanosomes.

2. Trypanosomes which had been subjected *in vitro* to the action of a 1/2,000 solution of Bayer 205 for two hours, when they are subsequently injected, either before or after washing, into a new animal, are not more sensitive to 15 mgm. of tartar emetic than are the normal trypanosomes.

3. Trypanosomes which had been subjected *in vitro* to the action of Bayer 205, and had then been washed three times and tested against various concentrations of tartar emetic, proved in half the cases to be more sensitive to the action of this drug than are the normal trypanosomes.

4. Trypanosomes which had been subjected to the action *in vitro* of Bayer 205, after having been washed three times, show in half the experiments a fragmentation which leads to their gradual disappearance. This phenomenon is due to the presence in the nutrient medium of the serum of certain sheep.

5. In another group of experiments, with the blood of different sheep, the fragmentation due to the Bayer 205 was manifest in the presence of only a single serum. This action was well-marked when the concentration of Bayer was 1/1,000 ; it was not evident when the concentration was 1/5,000.

6. It was always possible with the same serum to demonstrate the sensitization to tartar emetic after the action of 1/1,000 solution of Bayer. When the concentration of the solution of Bayer 205 was reduced to 1/5,000 the trypanosomes were found to be no more sensitive to tartar emetic than were the normal trypanosomes.

The paper closes with a theoretical discussion of the meaning of these results. *W. Y.*

VAN DEN BRANDEN (F.) & DUMONT (P.). Sur la conservation de la tryparsamide et du tryponarsyl en climat tropical. [**The Conservation of Tryparsamide and Tryponarsyl in the Tropics.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. Oct. 30. Vol. 12. No. 3. pp. 379–384.

The Ministry of the Colonies sent to the authors in May 1932 a series of samples of tryparsamide "Poulenc," and of tryponarsyl "Meurice," which had been in the Congo for various periods since December, 1927. It was desired to obtain information regarding the way in which these preparations had conserved their therapeutic properties during their long sojourn in the Tropics. The authors submitted the samples to chemical analysis and tested their toxicity in rabbits ; they reached the conclusion that both preparations had remained unchanged. [Other arsenical preparations examined by the same authors did not keep so well (*Bull. of Hyg.*, Vol. 7, p. 509).] *W. Y.*

RODHAIN (J.) & HENRY (E.). Essai d'activité trypanocide comparée des principaux neo-arsenobenzols novarsenobenzols d'usage courant en Belgique. [**Comparative Trypanocidal Activity of the Arsenobenzols in Use in Belgium.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. Oct. 30. Vol. 12. No. 3. pp. 359–369.

Evidence has accumulated which shows that the various brands of salvarsan and neosalvarsan exhibit different degrees of toxicity, and furthermore that therapeutic activity is not necessarily proportional to the degree of toxicity. Some specimens of neosalvarsan which are relatively feebly toxic possess good therapeutic properties.

The authors have tested and compared the toxic and therapeutic activities of the various neosalvarsans at present in use in Belgium; these are Neosalvarsan of Lucius and Hoecht's, which is considered to be the standard (League of Nations Committee, 1925); arsébényl Meurice, a Belgian product; and Rhodarsan and Novarsenobillon, French products. The tests were carried out on rats infected with two different strains of *T. brucei-pecaudi*, viz., virus Tumba and virus Madimba. Rats infected with Tumba die, as a rule, in 6 days, and those infected with Madimba in 12 to 20 days.

The general conclusions reached were that with large doses (0·1 gm. per kilo) novarsenobillon was inferior to the other products, and with small doses (0·01 gm. per kilo) arsébényl exhibited the most regular action; apart from these results nothing definite emerged. [In the reviewer's opinion it is not possible to draw any definite conclusions from this work as the number of rats employed was so small. The authors have made no allowance for the fact that individual rats vary. The same dose of the same drug given to a considerable number of rats does not always produce the same therapeutic result. Probably different rats excrete the drug with different degrees of rapidity.]

W. Y.

Morris (K. R. S.). **The Infection of a Guinea-Pig with *Trypanosoma congolense* and *T. gambiense* from the Bite of *Glossina longipalpis*.**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 129–138. With 3 charts & 1 fig.

The following summary is given :—

"1. A mixed infection of *T. gambiense* and *T. congolense* was established in a guineapig from the bite of a wild *Glossina longipalpis*.

"2. In the first and subsequent passages through guineapigs, *T. congolense* was predominant in the late stages of the infection and apparently was responsible for death; *T. gambiense* was usually the first trypanosome to appear, but remained in moderate numbers in peripheral blood.

"3. The infection was more virulent to *Cricetomys gambianus* than to *Mus rattus*; in both rats *T. congolense* was always swarming in the blood at death. *T. gambiense* only appearing in moderate numbers in the latter stages of the infection.

"4. The infection increased in virulence towards both rats and guineapigs in successive passages by injection.

"5. In a *M. rattus* that developed a septic tail after infection, the *T. gambiense* strain relapsed, but subsequently killed the rat." *W. Y.*

Regendanz (P.). Die experimentelle Erzeugung von Schlafkrankheit beim natürlich immunen Pavian durch Infektion des Liquor cerebrospinalis. [**Experimental Production of Sleeping Sickness in Naturally Immune Baboons by Infection of the Cerebrospinal Fluid.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Aug. Vol. 36. No. 8. pp. 409–425. With 10 figs. [19 refs.]

A brief summary of the literature is given indicating that baboons cannot be infected with the pathogenic trypanosomes of man and stock. The immunity of the baboon is due to trypanocidal antibodies present in the blood. These are not found in the cerebrospinal fluid, and consequently it occurred to Regendanz to see whether baboons could be infected by intralumbar injection of trypanosomes.

Baboon 1 was injected intrathecally with *T. gambiense* and 15 days later trypanosomes were found in the spinal fluid in large numbers. During the following few months parasites were only once found in the fluid, but a year later they were again found in great numbers, and again also during the 18th, 20th and 22nd months. An increase in the cell count was observed throughout the whole period. The animal died 2 years after the first injection with typical histological changes in the central nervous system.

Baboon No. 2 had repeated intrathecal injections of *T. rhodesiense*. There was no change in the cerebrospinal fluid and no trypanosomes were found. The animal was then injected with *T. gambiense* and a month later trypanosomes were found in the spinal fluid, but at later punctures they were not found. Throughout the whole period, however, there was an increased cell count. Death occurred a year after the injection of *T. gambiense*, and typical lesions were found in the nervous system.

Baboon No. 3 had one injection of *T. rhodesiense* and three of *T. gambiense*. Trypanosomes were never found in the spinal fluid, but the cell count was always increased. Death occurred a year after the first injection of *T. gambiense* and typical lesions were found in the brain.

Baboon No. 4 had six injections of *T. brucei*. No changes were found in the spinal fluid and at death, which occurred 10 months after the first injection, no lesions were found in the central nervous system, so the cause of death was not clear.

The author gives the following summary :—

Whilst infection of baboons is not possible through the blood stream, it occurs after direct inoculation of *T. gambiense* into the cerebrospinal fluid and a chronic infection results.

It remains limited to the spinal fluid ; a blood infection does not develop.

As a result of the cerebrospinal infection, the baboons develop cerebrospinal symptoms, which, however, are not so pronounced as in man. The animals died within one to two years.

The lesions in the brain correspond with those found in human sleeping sickness ; they are very pronounced.

The significance of these results for the understanding of the pathogenesis of human sleeping sickness is briefly considered, and the danger of lumbar puncture in the early stages of this disease is referred to.

The use of baboons is recommended for the testing of chemotherapeutic agents, especially as to their capacity to pass the meningeal barrier and act on trypanosomes in the cerebrospinal fluid. *W. Y.*

REICHENOW (Eduard). Das Verhalten von *Trypanosoma gambiense* in der Kultur. [**The Behaviour of** *T. gambiense* **in Culture.**]—*Ztschr. f. Parasitenk.* 1932. Sept. 5. Vol. 4. No. 4. pp. 784–793. [11 refs.]

It has been observed that in cultures of trypanosomes the blood forms disappear and are replaced by forms resembling the developmental forms seen in the gut of Glossina. Furthermore, it has been repeatedly stated that strains of *T. gambiense* which are maintained for long periods by passage through the vertebrate host gradually lose their capacity to infect the invertebrate host. These facts suggested to the author that the cause of the frequent failures to cultivate pathogenic trypanosomes successfully was due to the fact that the attempts were usually made with old laboratory strains which had lost the power either to develop

in the insect host or in the culture tube. This was the interpretation offered by RAZGHA [this *Bulletin*, Vol. 27, p. 244] to explain the fact that he was able to culture certain strains and not others.

Reichenow decided to repeat and extend RAZGHA's observations. A strain of *T. gambiense* (F), which was readily cultivated immediately after its isolation from man, was found to have lost its cultural capacity completely 3 years later ; and this was also the case when monkey or guineapig blood replaced human blood in the culture medium.

A second strain (*gambiense* G) freshly isolated from a patient was successfully cultured through 7 passages during a period of 111 days, and could presumably have been carried on indefinitely. The cultures showed, however, only forms similar to those met with in the gut of Glossina ; salivary gland forms were never found. The author believes that in order to produce the latter it would be necessary to alter the constitution of the nutrient medium ; but all his efforts in this direction have so far been fruitless. *W. Y.*

NATTAN-LARRIER (L.) & NOYER (B.). Action de l'ultrafiltration et de la chaleur sur le pouvoir trypanolytique des immun-sérums. [**Action of Ultrafiltration and of Heat on the Trypanolytic Power of Immune Serum.**]—*C. R. Soc. Biol.* 1932. Aug. 12. Vol. 110. No. 28. pp. 1237–1239.

In previous papers (this *Bulletin*, Vol. 29, p. 303 and p. 651), the authors have shown that collodion membranes retain both the protective substance and the curative anti-trypanosomal substance of immune sera. In the present work they have inquired firstly whether these membranes likewise hold back the trypanolytic substance of immune sera, and secondly whether heat had the same action on the trypanolytic power as on the protective power of immune sera.

The authors employed the commercially prepared membranes ; filtration was made at a negative pressure of 25 cm. of Hg. With membrane K600 the duration of filtration was 2 hours, and with membrane K250 it was 3 hours. The immune sera were obtained from rabbits infected with *T. marocanum* var. *cameli*. Four experiments showed clearly that the trypanolytic substance readily traverses both membranes K600 and K250. As a matter of fact the concentration of trypanolytic substance in the filtrate was considerably greater than that in the unfiltered serum.

Experiments on the thermostability of the trypanolytic substance showed that heating to 57°C. or 59°C. for 1 hour slightly diminished the trypanolytic action, but never destroyed it. *W. Y.*

EUFINGER (H.), ROTHERMUNDT (M.) & WIESBADER (H.). Das Verhalten der trypanociden Leberfunktion beim Uteruscarcinom und in der Gestationsperiode. [**The Behaviour of the Trypanocidal Liver Function in Uterine Carcinoma and Gestation.**]—Reprinted from *Arch. f. Gynäkol.* 1932. Vol. 151. Nos. 1 & 2. pp. 150–167. With 1 fig.

After briefly reviewing the literature relating to the disappearance or decrease of the trypanocidal substance from human serum in certain pathological conditions, the authors record a number of observations which they have made on the titre of this substance in the serum of pregnant women, of those suffering from eclampsia, and of cases of cancer of the uterus.

The formation of the trypanocidal substance is dependent upon a normal liver function. Decrease in the titre of this substance results from a partial functioning of the liver and especially from a generalized injury of the parenchyma. In cirrhosis of the liver, and in many cases of pernicious anaemia, there is pronounced decrease of trypanocidal substance. In genital cancer there is, as a rule, a slight degree of decrease in the trypanocidal body and this is related to an interference with liver function. Of 17 cases the trypanocidal titre was normal in 3, raised in 2 and much decreased in 12 cases. The two cases in which it was raised had recently been subjected to the influence of Röntgen rays ; and observations on the 12 cases in which the titre was lowered indicated that Röntgen rays resulted in an increase in liver function.

At the beginning of pregnancy there is a slight decrease in the trypanocidal titre, whilst during the last month of gestation there is a compensatory increase. In pregnancy intoxications—pregnancy nephritis, and eclampsia—there is, as a rule, no departure from the changes found in normal pregnancy ; only in occasional very severe cases is a decrease of the trypanocidal titre to be observed towards the end of pregnancy. *W. Y.*

v. Brand (Th.), Regendanz (P.) & Weise (W.). Der Milchsäuregehalt und die Alkalireserve des Blutes bei experimentellen Trypanosomeninfektionen. [**The Lactic Acid Content and the Alkali Reserve of the Blood in Experimental Trypanosomal Infections.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. Sept. 21. Vol. 125. No. 7/8. pp. 461–468. [13 refs.]

The authors have re-examined the question of the lactic acid content of the blood of rats and rabbits infected with trypanosomes. They found that it is only increased in the agonal or pre-agonal stages of the disease. This agonal increase is, moreover, not confined to trypanosomiasis ; it is seen for example in the Bartonella infections of splenectomized rats.

Notwithstanding the increase of the lactic acid content, the alkali reserve of the blood is not decreased in the agonal or pre-agonal stages of trypanosomal infections of rabbits.

The authors were unable to establish by *in vitro* experiments that trypanosomes in their metabolism produce lactic acid. *W. Y.*

Dunn (Lawrence H.). **Experiments in the Transmission of** *Trypanosoma hippicum* **Darling with the Vampire Bat,** *Desmodus rotundus murinus* **Wagner, as a Vector in Panama.**—*Jl. Preventive Med.* 1932. Sept. Vol. 6. No. 5. pp. 415–424.

The following summary is given :—

" 1. The positive results in five out of the six experiments in the transmission of " murrina " (the equine disease produced by *Trypanosoma hippicum* Darling) through the agency of the vampire bat, *Desmodus rotundus murinus* Wagner, definitely prove the vampire bat to be a vector of the disease.

" 2. The eight bats used readily acquired the disease, either by taking a meal of blood directly from an infected animal or by consuming blood that had previously been taken from an infected animal.

" 3. The incubation periods in the bats were from six to eight days.

" 4. The disease proved fatal to all the bats.

" 5. The interval between infection and death in the bats varied from nine to 27 days. Since the bats seem to feed every night, this long interval gives ample opportunity for them to bite many animals after they—the bats—have acquired the infection. The bats' appetite seems to be in no way impaired by the infection, but, on the contrary, increased, as is the case with equines that have the disease.

" 6. In the five experiments with positive results, the following clean animals became infected through the bites of vampire bats : 25 out of 55 guineapigs (45·4 per cent.), 3 out of 11 horses and mules (27·3 per cent.). One horse and one mule were each infected from a single bite.

" 7. In the light of our present knowledge concerning the vampire bat as a transmitter of " murrina " under natural conditions, it is recommended that equines be protected from the attacks of bats. Fortunately, protection from bats can be effected with greater ease than is the case with diptera or other arthropods. Adequate protection is provided by stabling the equines from the beginning of dusk to dawn in screened shelters, the wire mesh being not more than one inch, or by illuminating the stables with lanterns or electric light." *W. Y.*

REGENDANZ (P.). Ueber die Immunitätsvorgänge bei der Infektion der Ratten mit *Trypanosoma lewisi*. [**The Immunity Processes in** *T. lewisi* **Infections of Rats.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1932. Vol. 76. No. 6. pp. 437–445.

The essential difference between the course of the infection of trypanosmes of the *lewisi* group and that of the pathogenic trypanosomes is that in the former a short multiplication period is followed by a period of chronic infection in which divisional forms can no longer be discovered, whilst in the latter these well-defined periods are not observed. In the pathogenic infections there is either a progressive multiplication of the parasites up to the death of the host (*T. brucei* in mice) or an alternation of increase and decrease in the number of trypanosomes up to the end of the infection (*T. gambiense* in man, and *T. brucei* in the larger animals). The last condition is due to the development of antibodies by the host on the one part, and to the reaction of the parasite to these antibodies on the other.

Previous work by TALIAFERRO and by Regendanz and KIKUTH has shown that the termination of the divisional period of *lewisi* infections in rats is due to an antibody, and that this limits the multiplication of the parasites but is not trypanocidal ; and finally that this peculiar antibody is formed mainly in the spleen, because in rats splenectomized before infection the multiplication period was considerably prolonged. COVENTRY considered that in addition to these antibodies another trypanocidal antibody was formed.

Regendanz conducted a series of experiments in which the serum of rats, in the stage of chronic infection with *T. brucei*, was injected into rats at the beginning of the infection. From the results, which are given in a table, it appears that in only two of six rats in the first stage did a decrease or disappearance of parasites follow the injection of the serum of the chronically infected animals. Consequently, it appears doubtful whether COVENTRY'S contention that a trypanocidal substance is developed in the stage of chronic infection can be accepted.

There are certain analogies between the action of the immune serum and that of arsenophenylglycine. The effect of the drug depends

largely on the period of the infection when it is given (REICHENOW and Regendanz). Divisional forms are killed by small doses of the drug, whilst the adult monomorphic forms are uninfluenced. Furthermore, heavy infections require larger doses than do light infections; and finally it is noteworthy that doses which fail to cure infections of the first stage nevertheless suffice to bring multiplication to an end. Immune serum behaves in a similar manner.

Regendanz believes that the course of the infection of *T. lewisi* in rats is as follows. When the monomorphic adult trypanosomes are injected into a normal rat they commence to multiply because they are no longer in a medium containing the peculiar division-inhibiting antibody. In response to the infection this antibody is gradually formed, and finally the multiplication period is brought to an end. At the conclusion of this period there may be a decrease in the number of parasites because certain forms which have not yet completed their division are destroyed. In the second period, which lasts for weeks or months, only monomorphic adult forms are seen, because of the constant presence of the antibody. The parasites gradually die and finally the infection terminates.

As the result of a considerable series of experiments, which are summarized in a table, Regendanz was unable to confirm the statement of TALIAFERRO that, in Bartonella-free rats, splenectomy did not give rise to a severe infection. Regendanz believes that splenectomy alone suffices to lessen antibody formation and that consequently the course of the infection is more severe. *W. Y.*

TALIAFERRO (William H.). **Trypanocidal and Reproduction-inhibiting Antibodies to *Trypanosoma lewisi* in Rats and Rabbits.**—*Amer. Jl. Hyg.* 1932. July. Vol. 16. No. 1. pp. 32–84. [32 refs.]

The following summary is given :—

" 1. The trypanocidal property of the serum of rats having recovered from an infection with *T. lewisi*, as tested both curatively and protectively, shows the following characteristics :—

" (*a*) It is precipitated with the globulin fraction, sometimes with the euglobulin alone (tables 3 and 4) and sometimes with both the eu- and pseudoglobulin (tables 1 and 2).

" (*b*) It shows a marked *in vitro* affinity for both adult and dividing *T. lewisi* and can be removed from immune serum by absorption with the trypanosomes (table 5). Such trypanosomes after being in contact with immune serum are sensitized so that they are quickly killed when introduced into a normal previously uninfected rat.

" (*c*) A lysin can be demonstrated sporadically *in vitro* (table 6).

" 2. The reproduction-inhibiting property of serum from rats having recovered from an infection with *T. lewisi*, or from rats still infected but in which the trypanosomes have stopped all reproduction, has the following characteristics :—

" (*a*) Similar to the trypanocidal property it is precipitated with the globulin fraction, sometimes with the euglobulin alone (table 7) and sometimes with both the eu- and pseudoglobulin.

" (*b*) It is produced in rats as a result of immunization with injections of killed trypanosomes (table 9).

" (*c*) Unlike the trypanocidal property it shows no persistent *in vitro* affinity for either dividing or adult *T. lewisi* and cannot be removed from immune serum by absorption with trypanosomes (table 8). Similarly neither dividing nor adult trypanosomes are sensitized *in vitro* by treatment with serum containing the property.

" 3. The trypanocidal property and the reproduction-inhibiting property of immune serum can be separated by absorption with *T. lewisi* (table 10). In addition their *in vivo* activity on the parasites is strikingly different and one may be formed by a host without the other (table 17). The reproduction-inhibiting property seems to be a new type of antibody for which the name *ablastin* is proposed.

" 4. Both trypanocidal and reproduction-inhibiting antibodies play an important rôle in the immunity of recovered rats to a second infection with *T. lewisi* (tables 11, 12 and 13).

" 5. It is not clear whether the persistence of the trypanocidal and reproduction-inhibiting antibodies in the blood after apparent recovery is always associated with the persistence of a few trypanosomes in the body. In some cases, as the result of splenectomy and other treatment affecting the reticulo-endothelial system, the infection will relapse many months after an apparent cure (tables 14 and 15).

" 6. Immune serum from rabbits immunized with *T. lewisi* contains only the trypanocidal property and not the reproduction-inhibiting one (table 17). The trypanocidal property of such serum possesses the same properties listed under number 1 for the immune serum from rats (table 16)."

W. Y.

i. Dias (Emmanuel). Sur les déjections du *Triatoma megista*. Aspects du *Trypanosoma cruzi* que l'on y rencontre. [**The Dejecta of *T. megista*. Morphology of *T. cruzi* found therein.**]—*C. R. Soc. Biol.* 1932. Nov. 4. Vol. 111. No. 33. pp. 486–489. With 2 figs.

ii. ——. Expériences sur la transmission du *Trypanosoma cruzi* de l'insecte au vertébré. [**Transmission Experiments.**]—*Ibid.* pp. 490–492.

i. In Triatoma, as in all insects, there are two kinds of dejecta—the faeces and the malpighian excretion. The faeces are black and desiccate slowly. The urinary excretion is of two types: a yellowish turbid liquid, rich in crystals, and a colourless transparent liquid. In general, a few minutes after feeding, the Triatoma emits faeces or yellow urine; a little later it emits a fluid which may be perfectly clear or which contains faeces. At various intervals the insect continues to excrete clear dejecta. The day after the meal the urine becomes thick and yellow and contains numerous urate crystals. All subsequent dejecta exhibit these characters.

The chief interest of the clear urine is that when it comes from infected Triatoma it contains trypanosomes, sometimes very numerous. Examination showed that they are metacyclic forms; crithidial forms are always rare or absent. The metacyclic forms are very motile, thin and elongated; they are 17 μ in length, the nucleus is elongated and central or displaced posteriorly, and the blepharoplast is round and situated some distance from the posterior extremity. The metacyclic forms are capable of penetration and will infect if placed on the eye or on the undamaged skin of a guineapig.

ii. The author has attempted to infect guineapigs by allowing infective Triatoma to bite them, and by placing the clear malphigian excretion on the eyes and on the unbroken skin. Three guineapigs, which were bitten by infective insects, did not become infected, whilst the clear malphigian secretion containing metacyclic forms infected one guineapig when placed on the eye and three guineapigs when placed on the normal skin.

W. Y.

GREMEAU (R. P.). L'emploi d'un nouvel excipient de la tryparsamide : le sérum de cheval (hémostyl). [**Horse Serum as an Excipient of Tryparsamide.**]—*Rev. Méd. et Hyg. Trop.* 1932. July-Aug. Vol. 24. No. 4. pp. 176–179.

In this short article the author advocates, mainly on theoretical grounds, the use of dilute horse serum instead of water as an excipient for tryparsamide. *W. Y.*

VON JANCSÓ (N.). Wirkungsmechanismus der Chemotherapeutica bei Trypanosen. [**Mechanism of the Action of Chemotherapeutic Agents upon Trypanosomes.**]—*Klin. Woch.* 1932. July 30. Vol. 11. No. 31. pp. 1305–1307.

This paper repeats the experimental facts and conclusions fully described in previous papers by the author, and summarized in this *Bulletin*, Vol. 29, p. 646. *W. Y.*

CHATTON (Edouard). A propos du rôle de la membrane péritrophique des glossines dans l'évolution du trypanosome du crocodile, *T. Grayi* (=*T. Kochi*).—*Bull. Soc. Path. Exot.* 1932. June 8. Vol. 25. No. 6. pp. 575–577.

CLIMATIC BUBO AND LYMPHOGRANULOMA INGUINALE.

DE WOLF (H. F.) & VAN CLEVE (J. V.). **Lymphogranuloma Inguinale.** *Jl. Amer. Med. Assoc.* 1932. Sept. 24. Vol. 99. No. 13. pp. 1065–1070. With 4 figs. [35 refs.]

A general account of the disease which needs no comment, followed by a most interesting account of results obtained between August 1930 and March 1932 by Frei's skin test. These are summarized below.

1,010 persons in the Cleveland Hospital tested, 93 more than once. 58 yielded positive reactions; of these (*a*) 31 showed the clinical picture of L.I. 10 W.M.*; 20 C.M.; 1 C.F.

(*b*) 4 had been treated for the adenopathy previously but since recovered, 1 W.M.; 2 C.M.; 1 C.F.

(*c*) 20 gave a typical history of L.I. 19 W. and C.M.; 1 C.F.

(*d*) 3 cases of ano-rectal disease. 1 W.M.; 1 W.F.; 1 C.F.

11 upon whom 21 tests were made gave "confusing reactions," that is to say these were not definitely positive; none of these had signs or history of L.I. [A point which emphasises the necessity of only accepting frank positive reactions.] 941 were negative and had no manifestations nor history of the disease.

75 chancroid cases, 41 with buboes, 55 Ducrey bacillus positive, 22 W.M.; 46 C.M.; 3 W.F.; 5 C.F. 2 only gave positive L.I. skin test—one of these was a double infection with L.I.; the other had a history of adenitis 18 months before.

84 cases early active syphilis: 0 Frei positive. 58 cases frank gonorrhoea: 4 Frei positive; all gave a previous history of inguinal adenitis.

The ano-rectal cases consisted of (*a*) a white male who admitted forced sodomy while a prisoner in 1919; there was rectal stricture and anal growths but no inguinal adenitis and no penile scar. W.R. negative. (*b*) A white female who had cerebral syphilis but was smear negative for gonococcus. She had a rectal stricture 5 cm. above the anus. (*c*) A coloured woman with no evidence of gonorrhoea, no inguinal gland enlargement and negative Wassermann and Kline reactions. She showed rectal stricture, anal fistula and fistulous communication between a perirectal gland and the vagina together with signs of perimetritis. *H. S. Stannus.*

LUJÁN (Mario) & ROTTER (Werner). Lymphogranuloma inguinale bei Kindern. [**L.I. in Children.**]—*Klin. Woch.* 1932. Aug. 13. Vol. 11. No. 33. p. 1387.

A most instructive account of wholesale L.I. infections in a household at San José in Costa Rica. Two children (A and B) sisters, aged 6 and 7 years, developed bilateral inguinal adenopathy within a week of each other, the one with constitutional symptoms, the other without. In the one the gland masses were excised when the size of hen's eggs; in the other, in which they were the size of duck's eggs, resolution took place under treatment with electro-collargol. The father denied any venereal disease or gland swelling. A Frei skin reaction was not performed on him. The mother (C) denied venereal disease and an exhaustive examination revealed no clinical manifestations but the W.R. was positive and Frei test positive.

* W.M.=White male; C.M.=Coloured male; W.F.=White female; C.F.=Coloured female.

A 16-year-old daughter (D), *i.e.*, an elder sister of A and B, was found to have had inguinal buboes a year before. A girl cousin (E) of the mother who lived in the house had been operated on for the same complaint a year ago and been nursed by the mother (C). She had been infected by a man who was known to have had buboes. Two other female cousins (F and G) of the mother who also were in the house had also had buboes a year ago. Whether these two girls had contracted their disease venereally is unknown, but it seems certain that the two children A and B acquired their disease by simple contact with one of the other girls in bed or from the mother, "a carrier" who obtained infection by nursing her cousin E. *H. S. S.*

Amtman (Leo) & Pilot (I.). **Lymphogranuloma Inguinale. Report of Three Cases from Chicago.**—*Arch. Dermat. & Syph.* 1932. Nov. Vol. 26. No. 5. pp. 868–878. With 4 figs. [21 refs.]

A record of three cases of inguinal adenitis clinically resembling L.I. One had been in Nicaragua shortly before, the others were resident in Chicago. In none was there a history of primary lesion and exposure was denied. They all gave positive skin reactions with an antigen provided by Frei. *H. S. S.*

Sulzberger (Marion B.) & Wise (Fred). **Lymphopathia Venereum. (Lymphogranulomatosis Inguinalis of Nicolas, Favre and Durand.)** —*Jl. Amer. Med. Assoc.* 1932. Oct. 22. Vol. 99. No. 17. pp. 1407–1410. With 2 figs. [17 refs.]

A short general description of L.I. and some of those other conditions which have come lately to be regarded as due to infections with the virus of L.I.—elephantiasis of the genitals and rectal stricture.

[There is nothing new to be noted in this paper but attention is called to the following dictum—"The position of the stricture following Lymphopathia venereum is usually high in the rectum." This is a statement at complete variance with the observations of other authors who usually refer to the fact that it is "low." It is most commonly found 3–8 cm. above the anus. "Venereum" should surely be "venerea."] *H. S. S.*

Lutz (K.). Entzündliche Rektumstrikturen durch Lymphogranuloma inguinale. [**Inflammatory Rectal Stricture due to L.I.**]—*Deut. Med. Woch.* 1932. Aug. 26. Vol. 58. No. 35. pp. 1360–1361.

In this interesting clinical article are given the case notes of four women, all with practically the same history—increasing constipation, the passage of blood, mucus and pus by the bowel, ring stenosis of the rectum 3–5 cm. above the anus, with ulceration and papillomatous growths of the mucous membrane for some distance above the stricture and infiltration of the bowel wall. In one there was a cockscomb-shaped condyloma-like mass of perianal vegetations, in the second several periproctitic fistulae, in a third a recto-vaginal fistula. In all there was no evidence of syphilis but the intradermal reaction of Frei with L.I. antigen was positive. Dilatation by bougie, lavage and diathermy gave relief but no specific forms of treatment were essayed. *H. S. S.*

Caffé (L.) & Fulga (Costin). La phlébite du lympogranulome inguinal bénin. [**Phlebitis in L.I.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1932. July. Vol. 14. No. 7. pp. 501–503.

In a typical Frei positive case of L.I. four weeks after the appearance of the primary lesion and three weeks after the commencement of the adenitis, when the bubo was the size of an egg but before suppuration took place, the patient suffered sudden pain in the lower limb of the same side as the adenopathy, followed immediately by oedema and swelling. The femoral vein could be felt as a hard cord, leaving little doubt that the inflammatory process had spread directly from the matted mass of groin glands to the vein. *H. S. S.*

Löhe (H.) & Rosenfeld (H.). Neue Ergebnisse ueber die Spätformen des Lymphogranuloma inguinale (Esthiomène). [**Late Forms of L.I. (Esthiomene).**]—*Med. Klin.* 1932. Oct. 21. Vol. 28. No. 43 (1454). pp. 1486–1488. [14 refs.]

The authors believe that late manifestations of L.I. virus infections are less uncommon than was at one time supposed. They believe that genital elephantiasis or esthiomène may result from gland involvement due to sarcoma or carcinoma, tuberculosis and chancroid infections. The condition due to L.I. virus is predisposed to by a previous infection with syphilis. All their cases had had syphilis and most cases had a positive W.R. That the condition, esthiomène, is truly part of the disease they believe is proved by the following facts:—Meyer, Rosenfeld and Anders obtained an infection in a guineapig which could be passaged to the fourth animal with typical pathological picture by inoculation with tissue excised from such a patient. Reiss has published the case of a man developing typical Frei positive L.I. who had been living, but not having intercourse, with a prostitute who suffered from esthiomène and rectal stricture. An antigen prepared by Nicolas, Favre, Lebeuf and Charpy from pus of a case of the rectal disease gave positive skin tests in L.I. patients. Ravaut, Levaditi, Lambling and Cachera succeeded in infecting guineapigs with material from a rectal case and then passaging to a monkey by intracerebral inoculation, a monkey brain antigen giving a positive skin test in L.I. patients.

In association with Schlossberger and Koch further tissue was removed from the right nympha of the woman mentioned in the experiment by Meyer, Rosenfeld and Anders and used as inoculum into a monkey's brain. The animal developed symptoms in six weeks and died showing on post mortem examination a typical meningo-encephalitis. A brain antigen gave full positive reactions in 2 cases of L.I., mild positives in 2 other L.I. cases and negatives in 2 controls.

H. S. S.

Grippain (P.). Zur Therapie des Lymphogranuloma inguinale mit Introcid. [**Treatment of L.I. with Introcid.**]—*Muench. Med. Woch.* 1932. Sept. 16. Vol. 79. No. 38. pp. 1524–1525.

In view of disappointing results obtained by medical, surgical, radiological and vaccine methods of treatment the author has tried "Introcid," a preparation made by Desitin-Werk Carl Klinke, Hamburg and found useful in Hodgkin's disease and septic processes.

Three men with characteristic lesions and positive Frei skin reactions were given at 2–5 day intervals intravenous injections of 2–10 cc. with a total of 60cc with no general reactions. In one case gland masses the size of a fist in each groin quickly disappeared. In the other two, in which suppuration had already taken place, this treatment was combined with a small incision to evacuate the pus: the wounds healed in a short time and the infiltration cleared up rapidly. *H. S. S.*

Levaditi (C.), Ravaut (P.), Schoen (R.) & Vaisman (A.). Réceptivité du chat à l'égard du virus lymphogranulomateux de la maladie de Nicolas et Favre. [**Receptivity of the Cat to L.I. Virus.**]—*C. R. Soc. Biol.* 1932. Aug. 12. Vol. 110. No. 28. pp. 1218–1220.

A six weeks' old kitten, inoculated intracerebrally with a brain emulsion (0·5 cc.) from a monkey which had died on the 11th day after intracerebral inoculation of a brain emulsion from a mouse killed on the 122nd day after infection with Kamm strain of virus, was killed on the 9th day while still in apparent health.

Post mortem examination revealed an intense cortical meningitis; the pia was oedematous and infiltrated with polymorphonuclear cells, lymphocytes, a few plasma cells and large mononuclears; the polymorphonuclears and lymphocytes in separate masses; in the septa masses of karyolysed polynuclear cells formed miliary abscesses; there was also perivascular infiltration with lymphocytes and large mononuclears and an intense monocytic basal meningitis with involvement of cranial nerves and roots.

A monkey inoculated with an emulsion of this kitten's brain developed the characteristic reaction. Another kitten inoculated in the same way showed nervous symptoms on the 12th day and died the following day. *H. S. S.*

Jonesco-Mihaiesti, Tupa (A), Wismer (B.) & Badenski (G.). Syndrome aigu pseudo-tabétique à la suite de l'inoculation expérimentale de filtrat de lymphogranulome inguinal (Nicolas-Favre). [**Pseudo-Tabetic Syndrome following Inoculation of L.I. Virus.**]—*C. R. Acad. Sci.* 1932. Sept. 26. Vol. 195. No. 13. pp. 562–564.

An inoculum prepared from a gland, excised from a typical case of L.I., by grinding in saline with sand, filtration through paper and then passed successively through L.1. and L.2 Chamberland candles and proved sterile by ordinary tests, was injected transcranially into a *Macacus cynomolgus* monkey in dose of 5 cc. After an incubation period of 8 days the animal exhibited unsteadiness and inco-ordination followed by weakness, then complete paralysis with fibrillary twitchings —" a tetraplegia spasmodique "—and death. Post mortem examination revealed the usual changes in the brain and meninges. In the cord marked changes were found in the column of Goll, a systemization such as is seen in tabes. Degenerative changes in less degree were also present in the lateral columns and cerebellar tracts. The root ganglia and sciatic nerve showed similar infiltrative and degenerative changes but in less degree. No neurophagia was remarked such as is seen in poliomyelitis. Other animals in which this strain was passaged showed the same lesions. *H. S. S.*

FREI (W.). Zur Spezifität der Lymphogranuloma inguinale-Reaktion. [**Specificity of the L.I. Reaction.**]—*Dermat. Woch.* 1932. Oct. 29. Vol. 95. No. 44. pp. 1575–1582.

In this article, which might be read as supplementary to a previous paper by the same author (this *Bulletin*, Vol. 29, p. 731) Professor Frei returns to the question of specificity of the reaction which bears his name and treats the matter under three headings, (1) Positive reactions in cases which are not L.I. ; (2) Negative reactions in clinical cases of L.I. ; and (3) Positive reactions in L.I. patients with extraneous antigens.

Frei is more than ever convinced of the specificity of the reaction as his experience grows. He reaffirms the necessity of care in preparing antigen and in reading the result. He refers to CHEVALLIER'S case in which the use of an insufficiently heated antigen resulted in an infection. Allusion is also made to cases of latent infection without bubo which give a positive reaction.

In regard to (1) he points out that most of the false positive reactions are due to bacterial impurities in the insufficiently carefully prepared antigen and then goes on to deal specifically with the cases published by some of the Lyons workers as cases of non-specific reactions and shows the fallacies in their arguments.

That the reaction does not come off in 100 per cent. of cases of L.I. may be admitted ; as he has already pointed out in florid syphilis the reaction may be diminished or absent ; the same is true of possibly other conditions such as septicaemic processes and tuberculosis ; it is depressed sometimes in the premenstrual period and during high fever. Careful study of negative reactions is required and will probably go to enhance the value of the reaction.

Frei lays stress on the fact that L.I. patients react to all kinds of antigens more strongly than normals as a reason for rigid exclusion of other components than the specific antigenic substance from the antigen, and for this reason throws doubt upon the conclusions of WEISE and KLESTADT based upon 5 out of 7 positive reactions in L.I. patients using an antigen prepared from tissues removed from a case of elephantiasis vulvae. His opinion regarding the relationship of L.I. virus to elephantiasis vulvae is guarded.

The article should be read by everyone interested in this subject.

H. S. S.

GOTTLIEB (Filip). Neutralisation du virus de la lymphogranulomatose inguinale (maladie de Nicolas et Favre) par le sérum des malades en voie de guérison. Méthode de contrôle de l'intradermo-réaction de Frey. [**Neutralization of L.I. Virus by Serum of Recovering Patients.**]—*C. R. Soc. Biol.* 1932. Oct. 3. Vol. 111. No. 29. pp. 141–142.

Typical cases of L.I. were subjected to intradermal injections, as performed in Frei's skin test, using as inocula :—

1. An L.I. antigen prepared from pus or gland pulp—2 cases both positive.
2. The same mixed with saline—3 cases all negative.
3. A mixture of antigen and serum from healthy proved skin negative individuals—4 cases all positive.
4. Antigen and serum from L.I. patients who were recovering or had recovered from the adenitis commencing 3-6 months before—number of cases not stated but all negative.

An experiment which goes to prove that the serum of L.I. patients when they recover, acquires neutralizing properties against the L.I. antigen as used in Frei's intradermal test. *H. S. S.*

i. Gottlieb (Filip). Les manifestations articulaires au cours du lymphogranulome inguinal (maladie de Nicolas et Favre). [**Articular Manifestations in L.I.**] *Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1932. Oct. Vol. 14. No. 8. pp. 549–554.

ii. Liebreich (E.) & Gottlieb (F.). Lymphogranulome inguinal (maladie de Nicolas et Favre) accompagné d'arthrite, épisclérite et manifestations cutanées sous l'aspect d'érythème polymorphe. Cas de contagion conjugale. [**Arthritis, Episcleritis, and Skin Eruption in L.I. A Case of Conjugal Infection.**]—*Ibid.* pp. 554–561. With 2 figs.

i. The record of an L.I. infection, with intra-urethral primary lesion and a minor degree of adenopathy, but followed by marked swelling of one knee and pain also in elbows and wrists, thus resembling cases of L.I. associated with arthritis previously published by other authors. The author had had altogether 5 cases of arthritis among 48 patients.

ii. The record of a conjugal L.I. infection. The husband suffered a mild attack with primary sore and double inguinal adenitis, which cleared up in four months. His wife, whom he infected, was ill for eight months with double-sided bubo, multiple fistulae, marked general symptoms, muscular and articular pains, a polymorphous erythematous eruption on the forearms, arms, neck, trunk and lower limbs, each advance being accompanied by an exacerbation of pains and swelling in knees and feet and attacks of episcleritis. W.R. negative; gonorrhoea negative; Frei test positive. *H. S. S.*

Reiss (Franklin). Zur Frage der Infektiosität des sogen. genito-rectalen Syndroms als Spätfolge des Lymphogranuloma inguinale. [**Infectivity of the Genito-Rectal Syndrome in Later Stages of L.I.**]—*Klin. Woch.* 1932. Dec. 3. Vol. 11. No. 49. pp. 2031–2032.

Report of a case of a man 54 years old who developed Lymphogranuloma inguinale with a primary penile lesion. He had been living with a woman formerly a prostitute who was suffering from esthiomène and inflammatory stricture of the rectum. Both denied intercourse for two years past.

In the man Frei reaction positive; W.R. negative; Dmelcos reaction negative. In the woman Frei reaction positive; Dmelcos reaction negative; W.R. negative. The man had had gonorrhoea in the past; the woman had had gonorrhoea and syphilis in 1926, chancroid in 1927 and a bubo, 1928 gonorrhoea and chancroid at the anus (?), arthritis and pyelitis. Symptoms of rectal stricture began in 1927. *H. S. S.*

Zakon (S. J.). Lymphogranulomatosis Inguinalis or Durand-Nicolas-Favre Disease. [**L.I. A Review of the Literature.**]—*Arch. Dermat. & Syph.* 1932. Aug. Vol. 26. No. 2. pp. 238–249. With 4 figs. (3 coloured on 2 plates). [30 refs.]

After a brief review of some of the literature, the author gives notes of three cases seen while on a visit to Vienna. The article contains no new facts and was apparently written before the demonstration by Hellerström and Wassen of the presence of an ultra-microscopic virus.

H. S. S.

REVIEWS AND NOTICES.

MORISON (J.) [C.I.E., M.B., D.P.H., etc.]. **Bacteriophage in the Treatment and Prevention of Cholera.**—32 pp. With 27 figs. on 14 plates & 4 graphs. 1932. London: H. K. Lewis & Co. Ltd. [4s.]

Although the subject matter of this booklet deals specially with the preventive and curative treatment of cholera, it also sets out in an admirably clear manner some of the more theoretical and experimental aspects of the bacteriophage problem. No one will now deny the importance of the subject and its intimate connexion with bacteriology. The chemistry and architecture of the bacterium, the differentiation of bacterial species, recovery from and immunity to bacterial infection, chronicity of disease, the ebb and flow of epidemics, all these even to the very nature of living matter itself, are in one way or another bound up with the nature and activity of the bacteriophage. One of the most important chapters of the book is on the types of bacteriophage. D'HERELLE divided his bacteriophages into races and used this word for bacteriophages to avoid confusion with bacteria, for which the corresponding word " strain " was employed. " Races," says Morison, " in the present state of our knowledge are specific for certain bacteria or . . . for allied groups of bacteria." Races are subdivided into types and these again into sub-types. The first three types of cholera phage differentiated by ASHESHOV were named A, B and C. Morison and his co-workers have carried the alphabetical nomenclature as far as J. Perhaps the doubt that Z might be reached without the attainment of finality has been responsible for the mathematical expression of the mode of typing. With the isolation of more and more types the method has been evolved of employing strains of cholera vibrios made resistant to then known types, taken $(n-1)$ at a time, for diagnosis. Add to these, for the detection of a new type, a strain made resistant to all the n types, and we have a total of $(n+1)$ types. An important discovery for phage therapy with regard to types of bacteriophage is that natural mixtures of types are much more stable than the simple admixture of isolated pure types. The illustrations accompanying the dissertation on types of phage are numerous and excellent and give us all that is required for the understanding of the method of their isolation from a mixture. In his early work Morison obtained a combined bacteriophage which showed activity for both cholera and dysentery organisms. This is a particularly useful combination and especially where the two diseases are liable to occur concomitantly or even, as at El Tor, to be mistaken in the first instance the one for the other.

The conclusion has been reached that an efficient therapeutic phage must be of multi-type and should be maintained for use as nearly in its natural condition as possible. Such bacteriophages are " sought from as many patients as possible and from many samples of sewage."

Morison's observations, unfortunately only too short, on the subject of transmutation of cholera into cholera-like organisms are very interesting. " The bacteriophage," he says, " has something to do with the production of rough from smooth strains and *vice versa*. But we have so far been unable in the case of cholera to make agglutinable vibrios inagglutinable by growing them in the presence of bacteriophage. . . . We have further been unable to transform true cholera into " cholera-like " vibrios . . . under conditions that precluded contamination."

An original and noteworthy explanation of the natural history of epidemics of cholera in Assam is well deserving of attention. The fly-menace as a disseminator of cholera infection is summarily dismissed. Epidemic cholera in this province is a phenomenon of dying rivers and of the onset of monsoon rains, or at least of the rise of rivers. The dry, natural-latrine banks are washed over and the infection passes down stream to lower villages. This occurs in the first instance as a result of the melting of the Himalayan snows. The valley becomes infected and cholera breaks out.

Not only are we interested in this description of natural infection by the cholera organism but with the next phase which perhaps d'HERELLE would have called contamination with bacteriophage and subsidence of the epidemic. One might almost have expected to find that the bacteriophage derived from convalescent cholera cases, would have been transported by the swollen river to lower regions and so would bring epidemic conditions to an end by a water-borne agency. Apparently, however, the fall in cholera during July and August has been ascribed rather to dilution of the infection. It would seem also that this latter is not the author's own view. He is inclined to consider that " what brings cholera to a low ebb is the complete isolation of one village from another which is effected by the rain and the mud."

One more reference may be made to the important doctrinal matter contained in this essay. India is a land peculiarly suited to large scale trials and we await with interest the completion of the trial of bacteriophage, curatively for early cases of cholera and, by implication, prophylactically for the following epidemic. The district in Assam selected for test " has been free from cholera for a period twice as long as any during the last ten years." The graph given shows how striking is this immunity by contrast with the control district. Would that a control more closely resembling that of the alternate case type could have been instituted ! " We are entering, however, the fifth year since the last outbreak : Russell's periodic year for cholera in Assam. We have a population that is neither protected by recent cholera nor by vaccination. Until 1932 has passed we cannot be quite certain." The trial therefore is a crucial one and especially so in 1932 : it should, if it is convincing, go far to establish the usefulness not only of such trials but also of the forecasts which are now regularly made in respect of epidemic diseases in India.

W. F. Harvey.

VENEZUELA. **Estados Unidos de Venezuela.—Ministerio de Salubridad y de Agricultura y Cria. Conferencia Sanitaria Nacional de 1931.** [National Health Conference, Venezuela, 1931.]—691 pp. With numerous illustrations. 1932. Caracas : Tipografia Americana.

This volume is a full report of the proceedings of the Health Conference of Venezuela which took place in December 1931 and is devoted especially to the question of malaria in Venezuela. There is much interesting information scattered through its pages but at the same time the articles do not permit of abstracting. In fact, the report would, we think, be of greater ultimate value if judicious editing excluded unimportant and redundant matter. The report consists of five parts. The first records the official opening and closing, with the speeches delivered. The second comprises the bulk of the volume and contains the numerous reports from the various officials telling of the conditions in their several districts which influence the prevalence of malaria. In this are many excellent illustrations of the " beautiful hatcheries " (hermoso criadero) for mosquitoes which seem to abound. Part III is a copy of the correspondence sent to the head office. Part IV is the statistical section, but the returns are too subdivided already to be abstracted, and are mainly of local interest. The final section reproduces the minutes of the sessions and the resolutions passed.

H. H. S.

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